STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 134738

To: Kevin Weddington Location: rem/3c70 Art Unit: 1614 Friday, October 15, 2004 Case Serial Number: 10/758719	From: Beverly Shears Location: Remsen Bldg. RM 1A54 Phone: 571-272-2528 beverly.shears@uspto.gov

Search Notes

REM-3760

Access DB# 134738

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: K. Weddington Examiner #: 68082 Date: 10-7-04

Art Unit: 1614 Phone Number ~~30~~ 272-0587 Serial Number: 10/758,719

Mail Box and Bldg/Room Location: _____ Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need. MEJ

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Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: _____

Inventors (please provide full names): _____

Earliest Priority Filing Date: _____

**For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

A method for supplying ~~a~~ bioavailable methionine to a diary cow with the methyl ester of methionine

A method for improving milk obtained from a diary cow with the methyl ester of methionine

A method for improving the conditions of the diary cow with the methyl ester of methionine

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STAFF USE ONLY	Type of Search	Vendors and cost where applicable
Searcher: Beverly e 2528	NA Sequence (#)_____	STN ✓
Searcher Phone #: _____	AA Sequence (#)_____	Dialog _____
Searcher Location: _____	Structure (#) _____	Questel/Orbit: _____
Date Searcher Picked Up: _____	Bibliographic _____	Dr.Link _____
Date Completed: _____	Litigation _____	Lexis/Nexis _____
Searcher Prep & Review Time: _____	Fulltext _____	Sequence Systems _____
Clerical Prep Time: _____	Patent Family _____	WWW/Internet _____
Online Time: _____	Other _____	Other (specify) _____

PTO-1590 (1-2000)

Weddington
10/758719


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     FILE 'REGISTRY' ENTERED AT 15:31:38 ON 14 OCT 2004
                E "METHIONINE, METHYL ESTER"/CN 5
L1             1 S E3
                E METHIONINE/CN 5
L2             2 S E3
L3             1 S 4510-08-1/RN

L3   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2004 ACS on STN
RN   4510-08-1  REGISTRY
CN   Butanamide, 2-amino-4-(methylthio)-, (2S)- (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   Butanamide, 2-amino-4-(methylthio)-, (S)-
CN   Methioninamide, L- (8CI)
OTHER NAMES:
CN   L-Methioninamide
CN   L-Methionine amide
CN   Methioninamide
FS   STEREOSEARCH
MF   C5 H12 N2 O S
CI   COM
LC   STN Files:   BEILSTEIN*, BIOSIS, CA, CAOLD, CAPLUS, CASREACT, CSCHEM, PS,
       TOXCENTER, USPAT2, USPATFULL
         (*File contains numerically searchable property data)
DT.CA  CAplus document type:  Conference; Journal; Patent
RL.P   Roles from patents:  BIOL (Biological study); PREP (Preparation); PROC
       (Process); RACT (Reactant or reagent); USES (Uses); NORL (No role in
       record)
RLD.P  Roles for non-specific derivatives from patents:  BIOL (Biological
       study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
RL.NP  Roles from non-patents:  ANST (Analytical study); BIOL (Biological
       study); PREP (Preparation); PROC (Process); PRP (Properties); RACT
       (Reactant or reagent); NORL (No role in record)
RLD.NP Roles for non-specific derivatives from non-patents:  PRP (Properties);
       RACT (Reactant or reagent)

Absolute stereochemistry.
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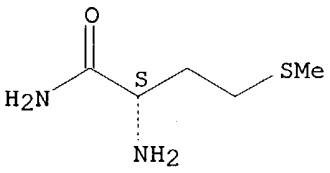


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**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

            154 REFERENCES IN FILE CA (1907 TO DATE)
              7 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
            154 REFERENCES IN FILE CAPLUS (1907 TO DATE)
              1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

     FILE 'CAPLUS' ENTERED AT 15:32:25 ON 14 OCT 2004
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Searcher : Shears 571-272-2528

L1 1 SEA FILE=REGISTRY ABB=ON PLU=ON "METHIONINE, METHYL ESTER"/CN

L2 2 SEA FILE=REGISTRY ABB=ON PLU=ON METHIONINE/CN
L3 1 SEA FILE=REGISTRY ABB=ON PLU=ON 4510-08-1/RN
L4 660 SEA FILE=CAPLUS ABB=ON PLU=ON L1 OR (METHIONINE OR MET)(3A)((ME OR METHYL)(W)ESTER)
L5 242 SEA FILE=CAPLUS ABB=ON PLU=ON L3 OR (METHIONINE OR MET)(W)AMIDE OR METHIONAMIDE
L6 5871 SEA FILE=CAPLUS ABB=ON PLU=ON (L2 OR MET OR METHIONINE) AND ESTER
L7 6 SEA FILE=CAPLUS ABB=ON PLU=ON (L4 OR L5 OR L6) AND ((DAIRY OR MILKING)(S)(COW OR CATTLE OR BOVINE OR (BOS OR B)(W)TAURUS))

L7 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 01 Feb 2004
ACCESSION NUMBER: 2004:80433 CAPLUS
DOCUMENT NUMBER: 140:145324
TITLE: Feed rations and methods of feeding growing ruminants
INVENTOR(S): Kunkle, William E.; Rodriguez, Edgar; Vazquez-Anon, Mercedes
PATENT ASSIGNEE(S): Novus International, Inc., USA
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004008874	A1	20040129	WO 2003-US322684		20030721
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
US 2004170669	A1	20040902	US 2003-623881		20030721
PRIORITY APPLN. INFO.:			US 2002-397156P	P	20020719
			US 2002-397957P	P	20020722

AB The present invention relates to feed rations, processes for formulating feed rations, and methods for improving weight gain in growing ruminants. The feed rations comprise a forage or other feed ingredient that meets daily nutritional requirements, other than **methionine**, and exceeds daily maintenance energy requirements of a growing ruminant. The feed rations further comprise an α-amino acid supplement, wherein the α-amino acid supplement is an analog of an α-amino acid.

IT **63-68-3**, L-**Methionine**, biological studies
63-68-3D, L-**Methionine**, **esters**, derivs. and salts
RL: FFD (Food or feed use); BIOL (Biological study); USES (Uses)

(feed rations and methods of feeding growing ruminants)
REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 01 Aug 2003
ACCESSION NUMBER: 2003:590714 CAPLUS
DOCUMENT NUMBER: 139:148557
TITLE: Protease catalyzed enantioselective oligomerization of α-hydroxy carboxylic acids and α-amino acids
INVENTOR(S): Lorbert, Stephen J.; Schasteen, Charles S.; Nam, Paul K.S.; Forciniti, Daniel; Rajesh, Mathur P.; Kapila, Shubhender
PATENT ASSIGNEE(S): Novus International, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 103 pp., Cont.-in-part of U.S. Ser. No. 699,946.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2003143661	A1	20030731	US 2002-136974		20020502
US 6605590	B1	20030812	US 2000-699946		20001030
US 2004048347	A1	20040311	US 2003-609825		20030630
PRIORITY APPLN. INFO.:			US 1999-162725P	P	19991029
			US 2000-699946	A2	20001030
			US 2001-288196P	P	20010502

OTHER SOURCE(S): MARPAT 139:148557
AB An enzymic synthesis and composition of oligomers and co-oligomers comprised of α-hydroxy carboxylic acids and α-amino acids or peptides is disclosed. In a preferred embodiment, a α-hydroxy carboxylic acid with a specific chiral configuration is linked by an amide linkage to a α-amino acid specific with a specific chiral configuration or linked by an amide linkage to a peptide made up of α-amino acid monomers having identical chiral configurations. Proteolytic enzymes catalyze oligomerization of the α-hydroxy carboxylic acid and α-amino acid. The degree and distribution of oligomerization varies upon the type and concns. of different reaction mixts. utilized and upon the length of allowed reaction time. The resultant oligomers may be provided to animals such as ruminants as bioavailable amino acid supplements that are resistant to degradation in the rumen and other animals such as swine, poultry and aquatic animals.
IT **63-68-3, L-Methionine**, reactions
RL: BCP (Biochemical process); RCT (Reactant); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent)
(protease catalyzed enantioselective oligomerization of α-hydroxy carboxylic acids and α-amino acids)

L7 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 08 Nov 2002

ACCESSION NUMBER: 2002:849901 CAPLUS
DOCUMENT NUMBER: 137:351937
TITLE: Enantioselective oligomerization of α-hydroxy carboxylic acids and α-amino acids, especially for rumen bypass and delayed digestion
INVENTOR(S): Lorbert, Stephen J.; Nam, Paul K. S.; Forciniti, Daniel; Rajesh, Mathur P.; Kapila, Shubhender
PATENT ASSIGNEE(S): Novus International, Inc., USA; Schasteen, Charles, S.
SOURCE: PCT Int. Appl., 148 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002088667	A2	20021107	WO 2002-US13708	20020502
WO 2002088667	A3	20030703		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-288196P P 20010502
OTHER SOURCE(S): MARPAT 137:351937

AB An enzymic synthesis and composition of oligomers and co-oligomers comprised of α-hydroxy carboxylic acids and α-amino acids or peptides is disclosed. In a preferred embodiment, an α-hydroxy carboxylic acid with a specific chiral configuration is linked by an amide linkage to an α-amino acid with a specific chiral configuration or linked by an amide linkage to a peptide made up of α-amino acid monomers having identical chiral configurations. Proteolytic enzymes catalyze oligomerization of the α-hydroxy carboxylic acid and α-amino acid. The degree and distribution of oligomerization varies upon the type and concns. of different reaction mixts. utilized and upon the length of allowed reaction time. The resultant oligomers may be provided to animals such as ruminants as bioavailable amino acid supplements that are resistant to degradation in the rumen and other animals such as swine, poultry and aquatic animals.

IT **59-51-8DP, Methionine,** 2-hydroxy-4-(methylthio)butyric acid derivs. **63-68-3DP, Methionine,** 2-hydroxy-4-(methylthio)butyric acid derivs.
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(enantioselective oligomerization of α-hydroxy carboxylic acids and α-amino acids, especially for rumen bypass and delayed digestion)

IT **63-68-3, L-Methionine,** reactions **63-68-3D, L-Methionine,** derivs.

RL: RCT (Reactant); RACT (Reactant or reagent)
(enantioselective oligomerization of α-hydroxy carboxylic acids and α-amino acids, especially for rumen bypass and delayed digestion)

L7 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 11 May 2001
ACCESSION NUMBER: 2001:338742 CAPLUS
DOCUMENT NUMBER: 134:352782
TITLE: Oligomers and oligomeric segments of α-hydroxy carboxylic acids and α-amino acids and uses in improving bioavailability of nutrition supplement for ruminants
INVENTOR(S): Lorbert, Stephen J.; Schasteen, Charles S.; Nam, Paul K. S.; Forciniti, Daniel; Rajesh, Mathur P.; Kapila, Shubhender
PATENT ASSIGNEE(S): Novus International, Inc., USA
SOURCE: PCT Int. Appl., 116 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001032906	A2	20010510	WO 2000-US29897	20001030
WO 2001032906	A3	20020214		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1224318	A2	20020724	EP 2000-976719	20001030
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				

PRIORITY APPLN. INFO.: US 1999-162725P P 19991029
WO 2000-US29897 W 20001030

OTHER SOURCE(S): MARPAT 134:352782

AB The invention is relates to the enzymic synthesis and composition of α-hydroxy carboxylic acid and α-amino acid or peptide co-oligomers wherein a residue of the α-hydroxy carboxylic acid is linked to a residue of the α-amino acid or peptide by an amide linkage. Proteolytic enzyme papain catalyzes co-oligomerization of the α-hydroxy carboxylic acid and α-amino acid. The degree and distribution of oligomerization varies upon the type and concns. of different reaction mixts. utilized and upon the length of allowed reaction time. The present invention is further directed to a process for the preparation of an oligomer. The process comprises preparing a mixture containing (i) an enzyme, (ii) an α-hydroxycarboxylic acid and (iii) an α-amino acid or a peptide oligomer. The α-hydroxy carboxylic acid and the α-amino acid each are present in the mixture as a free acid, acid

halide, amide, **ester** or anhydride independently of the other. The process further comprises forming an amide linkage between the residue of the α-hydroxy carboxylic acid and the residue of the α-amino acid or the peptide oligomer. The resultant oligomers may be provided to ruminants as bioavailable amino acid supplements that are resistant to degradation in the rumen.

IT **63-68-3, Methionine**, biological studies
RL: BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)
(2-hydroxy analog (MHBA), oligomerization of; oligomers and oligomeric segments of α-hydroxy carboxylic acids and α-amino acids and uses in improving bioavailability of nutrition supplement for ruminants)

L7 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 12 Feb 1999
ACCESSION NUMBER: 1999:90510 CAPLUS
DOCUMENT NUMBER: 130:138727
TITLE: Process for formulating ruminant feed using hydroxy analog of **methionine** for optimizing milk production
INVENTOR(S): Knight, Christopher D.; Koenig, Karen M.; Rode, Lyle M.; Vandenberg, Michael J.; Vazquez-Anon, Mercedes
PATENT ASSIGNEE(S): Novus International, Inc., USA
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9904647	A1	19990204	WO 1998-US15488	19980724
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6017563	A	20000125	US 1997-900414	19970725
AU 9885926	A1	19990216	AU 1998-85926	19980724
ZA 9806644	A	19990505	ZA 1998-6644	19980724
EP 998203	A1	20000510	EP 1998-937145	19980724
R: BE, DE, DK, ES, FR, GB, IT, LU, NL, MC, PT, IE				
JP 2001514841	T2	20010918	JP 2000-503726	19980724
EP 1354521	A1	20031022	EP 2003-14691	19980724
R: BE, DE, DK, ES, FR, GB, IT, LU, NL, MC, PT, IE				
US 6183786	B1	20010206	US 1999-333095	19990615
MX 200000810	A	20001027	MX 2000-810	20000124
US 6319525	B1	20011120	US 2000-697235	20001026
US 2002058085	A1	20020516	US 2001-990677	20011116
PRIORITY APPLN. INFO.:			US 1997-900414 A	19970725
			EP 1998-937145 A3	19980724

WO 1998-US15488 W 19980724
US 1999-333095 A1 19990615
US 2000-697235 A1 20001026

AB A process for formulating a ruminant feed in which the **methionine** needs of the ruminant are determined and adequate natural or synthetic feed ingredients are used, wherein one of said ingredients is 2-hydroxy-4-(methylthio)butanoic acid or a salt, amide or **ester** thereof, and a ration is formulated from the identified feed ingredients to meet the determined **methionine** needs of the ruminant which comprises one or more grains, a hydroxy analog of **methionine**, and optionally a bypass fat wherein (i) the hydroxy analog of **methionine** is selected from the group consisting of 2-hydroxy-4-(methylthio)butanoic acid and the salts, amides and **esters** thereof, (ii) the hydroxy analog of **methionine** is added sep. from any bypass fat which is included in the ration, and (iii) the ration is formulated on the basis that at least 20 % of the hydroxy analog of **methionine** is assumed to be available for absorption by the ruminant.

IT **63-68-3, Methionine**, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(process for formulating ruminant feed ration using 2-hydroxy-4-(methylthio)butanoic acid for sufficient **methionine** intake for milk production)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 12 May 1984
ACCESSION NUMBER: 1974:106326 CAPLUS
DOCUMENT NUMBER: 80:106326
TITLE: Metabolism of glucose, acetate, lipids and amino acids in lactating **dairy cows**
AUTHOR(S): Bickerstaffe, R.; Annison, E. F.; Linzell, J. L.
CORPORATE SOURCE: Unilever Res. Lab., Sharnbrook/Bedford, UK
SOURCE: Journal of Agricultural Science (1974), 82, Pt. 1, 71-85
CODEN: JASIAB; ISSN: 0021-8596
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The rates of entry into the circulation as determined by isotope dilution, of glucose, acetate, and plasma free fatty acids were 3.3-4.0, 1.7-2.1, and 0.5 kg/day, resp. Acetate and glucose contributed 32-50 and 4-11%, resp., of the total CO2 output by the animal. Measurement of the uptake of precursors of milk constituents and their transfer into milk showed that there were substantial arteriovenous differences of glucose, acetate, triglyceride, and β-hydroxybutyrate which were not significantly different between breeds or related to milk yield. Isotopic and balance data confirm that glucose is the main precursor of lactose and that the oxidation and transfer of glucose into lactose accounted for 69-98% of the glucose entry rate. As in the goat, plasma triglycerides and blood acetate accounted for 35-80% and 25-50% of the milk triglycerides, resp. Propionate was extracted from plasma but the uptake was only .apprx. 8% of the value for acetate. There was no net arteriovenous difference of

phospholipids, cholesterol **esters**, or free fatty acids, but the fall in sp. radioactivity of free fatty acids across the mammary gland indicated there was an exchange of free fatty acids between plasma and mammary tissue. In contrast to the lactating goat, cow plasma contained very few chylomicrons. The majority of the triglycerides taken up by the udder were derived from the low-d.-lipoprotein fraction. The essential amino acids were extracted from blood in amts. sufficient to account for the essential amino acids secreted into milk protein. Although the plasma level of **methionine** was low, 52-72% of the material reaching the mammary gland was taken up. The uptake of arginine was far in excess of the requirement for milk protein synthesis.

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO, CABA, AGRICOLA, VETU, VETB' ENTERED AT 15:36:39 ON 14 OCT 2004)
L8 16 S L7
L9 15 DUP REM L8 (1 DUPLICATE REMOVED)

L9 ANSWER 1 OF 15 WPIDS COPYRIGHT 2004 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-214286 [20] WPIDS
DOC. NO. CPI: C2004-084782
TITLE: Improving weight gain of growing ruminant comprises providing ruminant with feed ingredient(s) and -amino acid analog such that amounts consumed by ruminant in one day can collectively satisfy ruminant's daily nutrient requirements.
DERWENT CLASS: B05 C03 D13
INVENTOR(S): KUNKLE, W E; RODRIGUEZ, E; VAZQUEZ-ANON, M; MILLER, B G
PATENT ASSIGNEE(S): (NOVU-N) NOVUS INT INC; (KUNK-I) KUNKLE W E; (MILL-I) MILLER B G; (RODR-I) RODRIGUEZ E; (VAZQ-I) VAZQUEZ-ANON M
COUNTRY COUNT: 105
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2004008874	A1	20040129	(200420)*	EN	58
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW					
AU 2003252079	A1	20040209	(200450)		
US 2004170669	A1	20040902	(200458)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 2004008874	A1		WO 2003-US22684	20030721
AU 2003252079	A1		AU 2003-252079	20030721
US 2004170669	A1	Provisional	US 2002-397156P	20020719
		Provisional	US 2002-397957P	20020722
			US 2003-623881	20030721

FILING DETAILS:

Searcher : Shears 571-272-2528

PATENT NO	KIND	PATENT NO
AU 2003252079	A1 Based on	WO 2004008874

PRIORITY APPLN. INFO: US 2002-397957P 20020722; US 2002-397156P 20020719; US 2003-623881 20030721

AN 2004-214286 [20] WPIDS

AB WO2004008874 A UPAB: 20040324

NOVELTY - Improving weight gain of a growing ruminant comprises providing the ruminant with feed ingredient(s) and an -amino acid analog. The assortment and composition of the feed ingredients are such that the amounts, which can be consumed by the growing ruminant in one day, can collectively satisfy the ruminant's daily nutrient requirements, and exceed its daily maintenance energy requirements.

DETAILED DESCRIPTION - Improving weight gain of a growing ruminant comprises providing the ruminant with feed ingredient(s) and an -amino acid analog consisting of 2-hydroxy-4-(methylthio)butanoic acid, or their salts, **esters**, amides, ethers, diesters, **ester**/ethers, oligomers, metal chelates, or anion salts, or salt, **ester**, amide, ether, oligomer, metal chelate, or anion salt analogs of **methionine**. The assortment and composition of the feed ingredients are such that the amounts, which can be consumed by the growing ruminant in one day, can collectively satisfy the ruminant's daily nutrient requirements, and exceed its daily maintenance energy requirements, provided that such assortment and composition may not satisfy the ruminant's **methionine** requirements. The salts of 2-hydroxy-4-(methylthio)butanoic acid consist of ammonium, magnesium, lithium, sodium, potassium, or zinc.

INDEPENDENT CLAIMS are also included for:

(1) a process of formulating a feed ration for growing ruminants, comprising determining the nutritional requirements of the growing ruminant; determining the maintenance energy requirements of the growing ruminant; identifying feed ingredient(s) other than -amino acid analogs and determining the nutritional content and energy contribution of each of the feed ingredients; formulating a feed ration from the identified feed ingredients such that the amount of feed ration which can be consumed by the growing ruminant in one day can collectively satisfy the ruminant's daily nutrient requirements, and exceed its daily maintenance energy requirements, provided that such assortment and composition may not satisfy the ruminant's **methionine** requirements; and additionally incorporating into the feed ration an -amino acid analog without regard to its energy contribution to the feed ration; and

(2) a feed ration for growing ruminants comprising feed ingredient(s) and an -amino acid analog, and comprising at least 50% forage.

ACTIVITY - Anabolic.

MECHANISM OF ACTION - None given.

USE - For improving weight gain of a growing ruminant, e.g. growing beef or **dairy cattle** (claimed).

ADVANTAGE - The method consistently results in improving weight gain in growing ruminants, thus being beneficial to the productivity of the ruminant industry.

Dwg.0/1

L9 ANSWER 2 OF 15 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on

STN
ACCESSION NUMBER: 2004:802528 SCISEARCH
THE GENUINE ARTICLE: 850KQ
TITLE: The isopropyl **ester** of **methionine** hydroxy-analogue is absorbed through the rumen wall in the cow
AUTHOR: Graulet B; Richard C; Robert J C (Reprint)
CORPORATE SOURCE: ADISSEO France SAS, CERN, F-03100 Commentry, France (Reprint); ADISSEO France SAS, Dept Res & Dev, F-92160 Antony, France
COUNTRY OF AUTHOR: France
SOURCE: JOURNAL OF ANIMAL AND FEED SCIENCES, (SEP 2004) Vol. 13, Supp. [1], pp. 269-272.
Publisher: KIELANOWSKI INST ANIMAL PHYSIOLOGY NUTRITION, UL INSTYTUCKA 3, 05-110 JABLONNA, POLAND.
ISSN: 1230-1388.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 9

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB A new form of **methionine**, the isopropyl **ester** of **methionine** hydroxy analog (HMBi), has been proven to be available for milk protein synthesis in **dairy cows**. Studies have also shown that HMBi can be degraded by rumen micro-organisms. By two different experimental approaches (emptied and washed rumen; catheterization of the ruminal vein), we have demonstrated that HMBi ability to be rapidly absorbed by the rumen wall can explain its partial protection from microbial degradations. The high efficiency of HMBi to pass through biological membranes seems to be due to the molecule's isopropyl **ester** radical.

L9 ANSWER 3 OF 15 WPIDS COPYRIGHT 2004 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-855880 [80] WPIDS
DOC. NO. CPI: C2003-241629
TITLE: Animal feed supplement, in solid form, particularly used for ruminants, e.g. cow, comprises 2-hydroxy-4-(methylthio)butanoic acid.
DERWENT CLASS: D13
INVENTOR(S): DOLLAT, J; ROBERT, J; CHIAVAZZA, V
PATENT ASSIGNEE(S): (AVET) AVENTIS ANIMAL NUTRITION SA; (ADIS-N) ADISSEO FRANCE SAS
COUNTRY COUNT: 104
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 1358805	A1	20031105	(200380)*	EN	11
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR					
WO 2003092403	A1	20031113	(200402)	EN	
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU					

ZA ZM ZW
AU 2003225485 A1 20031117 (200442)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 1358805	A1	EP 2002-356081	20020430
WO 2003092403	A1	WO 2003-IB1726	20030428
AU 2003225485	A1	AU 2003-225485	20030428

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003225485	A1 Based on	WO 2003092403

PRIORITY APPLN. INFO: EP 2002-356081 20020430
AN 2003-855880 [80] WPIDS
AB EP 1358805 A UPAB: 20031211
NOVELTY - An animal feed supplement in solid form comprises 2-hydroxy-4-(methylthio)butanoic acid or its **ester** and a porous carrier material. The 2-hydroxy-4-(methylthio)butanoic acid or its **ester** is present at at least 20 weight% of the total composition of the feed supplement.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for an animal feed comprising the feed supplement.

USE - For animal feed (claimed), particularly for ruminants, e.g. cow.

ADVANTAGE - The invention shows good bioavailable results at least equivalent to the liquid form. It does not only provide large amount of **methionine** by also **methionine** is found to be present in the bloodstream after a short period of time.

DESCRIPTION OF DRAWING(S) - The figure shows blood plasma **methionine** concentration of **dairy cows** fed various **methionine**-supplying feed supplement.

Dwg.1/1

L9 ANSWER 4 OF 15 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2003:376808 SCISEARCH
THE GENUINE ARTICLE: 669CW
TITLE: Enzymatic synthesis and characterization of L-**methionine** and 2-hydroxy-4-(methylthio)butanoic acid (HMB) co-oligomers
AUTHOR: Rajesh M; Kapila S (Reprint); Nam P; Forciniti D; Lorbert S; Schasteen C
CORPORATE SOURCE: Univ Missouri, Ctr Environm Sci & Technol, 1870 Miner Circle, Rolla, MO 65409 USA (Reprint); Univ Missouri, Ctr Environm Sci & Technol, Rolla, MO 65409 USA; Univ Missouri, Dept Chem, Rolla, MO 65409 USA; Novus Int Inc, St Charles, MO 63304 USA
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY, (23 APR 2003) Vol. 51, No. 9, pp. 2461-2467.
Publisher: AMER CHEMICAL SOC, 1155 16TH ST, NW,

WASHINGTON, DC 20036 USA.
ISSN: 0021-8561.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 25
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Oligomers of L-**methionine** (**Met**) and its hydroxy analogue, 2-hydroxy-4-(methylthio)butanoic acid (D,L-HMB) were synthesized with the proteolytic enzyme papain. The **Met** homooligomers and HMB-**Met** co-oligomers obtained through the enzymatic reactions were subjected to persulfonation and separated with reverse phase liquid chromatography (RPLC). The separated oligomers were characterized with electrospray ionization-mass spectrometry (ESI-MS). The oligomers were also characterized with matrix-assisted laser desorption ionization time of flight mass spectrometry (MALDI-TOF-MS). The results showed that co-oligomers were predominantly composed of 4-8 **Met** residues and one HMB residue. The data also suggest that in the co-oligomers, HMB is attached at the N-terminal end of the oligopeptide chain.

L9 ANSWER 5 OF 15 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2002:594330 BIOSIS
DOCUMENT NUMBER: PREV200200594330
TITLE: Influence of 2-hydroxy-4 (methyl thio) butanoic acid isopropyl **ester** (HMBi) on the digestibility of organic matter and energy value of corn silage measured in vitro.
AUTHOR(S): Robert, J. C. [Reprint author]; Ballet, N. [Reprint author]; Richard, C. [Reprint author]; Bouza, B. [Reprint author]
CORPORATE SOURCE: Aventis Animal Nutrition, Antony, France
SOURCE: Journal of Dairy Science, (2002) Vol. 85, No. Supplement 1, pp. 240. print.
Meeting Info.: Meeting of the American Society of Animal Science and the American Dairy Science Association. Quebec City, Quebec, Canada. July 20-25, 2002. American Society of Animal Science; American Dairy Science Association.
CODEN: JDSCAE. ISSN: 0022-0302.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 20 Nov 2002
Last Updated on STN: 20 Nov 2002

L9 ANSWER 6 OF 15 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2002:568524 BIOSIS
DOCUMENT NUMBER: PREV200200568524
TITLE: Quantifying the metabolisable **methionine** contribution of a liquid or powder presentation of 2-hydroxy-4 (methylthio) butanoic acid isopropyl **ester** (HMBi).
AUTHOR(S): Robert, J. C. [Reprint author]; D'Alfonso, T. [Reprint author]; Etave, G. [Reprint author]; Depres, E. [Reprint author]; Bouza, B. [Reprint author]
CORPORATE SOURCE: Aventis Animal Nutrition, Antony, France

SOURCE: Journal of Dairy Science, (2002) Vol. 85, No. Supplement 1, pp. 71. print.
Meeting Info.: Meeting of the American Society of Animal Science and the American Dairy Science Association. Quebec City, Quebec, Canada. July 20-25, 2002. American Society of Animal Science; American Dairy Science Association.
CODEN: JDSCAE. ISSN: 0022-0302.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Nov 2002
Last Updated on STN: 7 Nov 2002

L9 ANSWER 7 OF 15 WPIDS COPYRIGHT 2004 THE THOMSON CORP on STN
ACCESSION NUMBER: 2001-355328 [37] WPIDS
CROSS REFERENCE: 2003-129141 [12]
DOC. NO. CPI: C2001-110103
TITLE: Preparation of an oligomer, used for the delivery of amino acids to ruminant animals, comprises preparing a mixture containing an enzyme, an alpha-hydroxy carboxylic acid and an alpha-amino acid or a peptide and forming an oligomer.
DERWENT CLASS: A23 A97 B05 C03 D13 D16 E19
INVENTOR(S): FORCINITI, D; KAPILA, S; LORBERT, S J; NAM, P K S; RAJESH, M P; SCHASTEEN, C S
PATENT ASSIGNEE(S): (NOVU-N) NOVUS INT INC; (FORC-I) FORCINITI D; (KAPI-I) KAPILA S; (LORB-I) LORBERT S J; (NAMP-I) NAM P K S; (RAJE-I) RAJESH M P; (SCHA-I) SCHASTEEN C S
COUNTRY COUNT: 92
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001032906	A2	20010510	(200137)*	EN	115
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW					
AU 2001014454	A	20010514	(200149)		
EP 1224318	A2	20020724	(200256)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
US 2003143661	A1	20030731	(200354)		
US 6605590	B1	20030812	(200355)		
MX 2002004226	A1	20030101	(200373)		
US 2004048347	A1	20040311	(200419)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001032906	A2	WO 2000-US29897	20001030
AU 2001014454	A	AU 2001-14454	20001030
EP 1224318	A2	EP 2000-976719	20001030

			WO 2000-US29897	20001030
US 2003143661	A1	Provisional	US 1999-162725P	19991029
		CIP of	US 2000-699946	20001030
		Provisional	US 2001-288196P	20010502
			US 2002-136974	20020502
US 6605590	B1	Provisional	US 1999-162725P	19991029
			US 2000-699946	20001030
MX 2002004226	A1		WO 2000-US29897	20001030
			MX 2002-4226	20020426
US 2004048347	A1	Provisional	US 1999-162725P	19991029
		Div ex	US 2000-699946	20001030
			US 2003-609825	20030630

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2001014454	A Based on	WO 2001032906
EP 1224318	A2 Based on	WO 2001032906
MX 2002004226	A1 Based on	WO 2001032906
US 2004048347	A1 Div ex	US 6605590

PRIORITY APPLN. INFO: US 1999-162725P 19991029; US 2000-699946 20001030; US 2001-288196P 20010502; US 2002-136974 20020502; US 2003-609825 20030630

AN 2001-355328 [37] WPIDS

CR 2003-129141 [12]

AB WO 200132906 A UPAB: 20040318

NOVELTY - Preparation of an oligomer comprises:

(a) preparing a mixture containing an enzyme, an alpha -hydroxy carboxylic acid and an alpha -amino acid or a peptide; and

(b) forming an oligomer in the mixture which contains a residue of the alpha -hydroxy carboxylic acid linked to a residue of the alpha -amino acid by an amide linkage.

DETAILED DESCRIPTION - The alpha -hydroxy carboxylic acid and alpha -amino acid are present as a free acid, acid halide, amide, **ester** or anhydride.

INDEPENDENT CLAIMS are also included for:

(A) a composition comprising the segment CA(AA)n; and

(B) a composition comprising a carboxylic acid derivative of formula (I):

CA = residue of an alpha -hydroxy carboxylic acid;

R1, R3 = H, or optionally substituted hydrocarbyl;

R2 = H, optionally substituted hydrocarbyl or a hydroxy protecting group;

AA = alpha -amino acid residue; and

n = at least 1.

With the proviso that CA is bonded to AA by an amide linkage

ACTIVITY - Anabolic.

No biological data is given.

MECHANISM OF ACTION - None given.

USE - The process is used for the preparation of oligomers, especially (I). (I) is used for providing an animal, preferably a ruminant, especially **dairy** (optionally lactating) or beef

cattle, with its nutritional or pharmacological amino acid needs (all claimed).

ADVANTAGE - The process produces oligomers, which are resistant to degradation in the rumen. No dosage is given.

Dwg.0/62

L9 ANSWER 8 OF 15 WPIDS COPYRIGHT 2004 THE THOMSON CORP on STN

ACCESSION NUMBER: 2000-387565 [33] WPIDS

DOC. NO. CPI: C2000-117591

TITLE: **Methionine** delivery useful in **dairy** production and **bovine** husbandry involves giving **methionine esters** and amides and/or **methionine** hydroxy analogue **esters** to **cows.**

DERWENT CLASS: B05 C03 D13 E16

INVENTOR(S): BENNETT, R; GROS, G; ROBERT, J; ROBERT, J C; WILLIAMS, P

PATENT ASSIGNEE(S): (RHON) RHONE-POULENC ANIMAL NUTRITION SA; (AVET) AVENTIS ANIMAL NUTRITION SA; (ADIS-N) ADISSEO IRELAND LTD; (RHON) RHONE-POULENC NUTRITION ANIMALE; (BENN-I) BENNETT R; (GROS-I) GROS G; (ROBE-I) ROBERT J

COUNTRY COUNT: 91

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000028835	A1	20000525	(200033)*	EN	30
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW					
FR 2785772	A1	20000519	(200033)		
FR 2785773	A1	20000519	(200033)		
AU 2000013854	A	20000605	(200042)		
US 6221909	B1	20010424	(200125)		
US 2001008904	A1	20010719	(200143)		
NO 2001002355	A	20010713	(200148)		
EP 1128738	A1	20010905	(200151)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
BR 9915290	A	20010807	(200152)		
CN 1326322	A	20011212	(200225)		
KR 2001099798	A	20011109	(200229)		
US 6372788	B1	20020416	(200232)		
US 2002103258	A1	20020801	(200253)		
JP 2002529108	W	20020910	(200274)		32
ZA 2001003539	A	20021030	(200282)		38
US 6528541	B2	20030304	(200320)		
US 2003143260	A1	20030731	(200354)		
NZ 511427	A	20030725	(200357)		
MX 2001004747	A1	20020601	(200365)		
EP 1128738	B1	20040512	(200431)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
DE 69917314	E	20040617	(200440)		
EP 1442664	A1	20040804	(200451)	EN	

R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
US 2004154549 A1 20040812 (200454)

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 2000028835	A1		WO 1999-EP9021	19991110
FR 2785772	A1		FR 1998-14249	19981113
FR 2785773	A1		FR 1999-10050	19990729
AU 2000013854	A		AU 2000-13854	19991110
US 6221909	B1		US 1999-438521	19991112
US 2001008904	A1	Cont of	US 1999-438521	19991112
			US 2001-794347	20010228
NO 2001002355	A		WO 1999-EP9021	19991110
			NO 2001-2355	20010511
EP 1128738	A1		EP 1999-972074	19991110
			WO 1999-EP9021	19991110
BR 9915290	A		BR 1999-15290	19991110
			WO 1999-EP9021	19991110
CN 1326322	A		CN 1999-813267	19991110
KR 2001099798	A		KR 2001-705853	20010509
US 6372788	B1	Cont of	US 1999-438521	19991112
			US 2001-794347	20010228
US 2002103258	A1	Cont of	US 1999-438521	19991112
		Cont of	US 2001-794347	20010228
			US 2002-60327	20020201
JP 2002529108	W		WO 1999-EP9021	19991110
			JP 2000-581896	19991110
ZA 2001003539	A		ZA 2001-3539	20010502
US 6528541	B2	Cont of	US 1999-438521	19991112
		Cont of	US 2001-794347	20010228
			US 2002-60327	20020201
US 2003143260	A1	Cont of	US 2002-60327	20020201
			US 2003-336912	20030106
NZ 511427	A		NZ 1999-511427	19991110
			WO 1999-EP9021	19991110
MX 2001004747	A1		WO 1999-EP9021	19991110
			MX 2001-4747	20010510
EP 1128738	B1		EP 1999-972074	19991110
			WO 1999-EP9021	19991110
DE 69917314	E		DE 1999-617314	19991110
			EP 1999-972074	19991110
			WO 1999-EP9021	19991110
EP 1442664	A1	Div ex	EP 1999-972074	19991110
			EP 2004-10767	19991110
US 2004154549	A1	Cont of	US 1999-438521	19991112
		Cont of	US 2001-794347	20010228
		Cont of	US 2002-60327	20020201
		Cont of	US 2003-336912	20030106
			US 2004-758719	20040116

FILING DETAILS:

PATENT NO	KIND	PATENT NO

Searcher : Shears 571-272-2528

AU 2000013854	A	Based on	WO 2000028835
US 2001008904	A1	Cont of	US 6221909
EP 1128738	A1	Based on	WO 2000028835
BR 9915290	A	Based on	WO 2000028835
US 6372788	B1	Cont of	US 6221909
JP 2002529108	W	Based on	WO 2000028835
US 6528541	B2	Cont of	US 6221909
		Cont of	US 6372788
US 2003143260	A1	Cont of	US 6528541
NZ 511427	A	Based on	WO 2000028835
MX 2001004747	A1	Based on	WO 2000028835
EP 1128738	B1	Based on	WO 2000028835
DE 69917314	E	Based on	EP 1128738
		Based on	WO 2000028835
EP 1442664	A1	Div ex	EP 1128738
US 2004154549	A1	Cont of	US 6221909
		Cont of	US 6372788
		Cont of	US 6528541

PRIORITY APPLN. INFO: FR 1999-10050 19990729; FR 1998-14249 19981113

AN 2000-387565 [33] WPIDS

AB WO 200028835 A UPAB: 20040418

NOVELTY - Giving bioavailable **methionine esters** or amides, **methionine** hydroxy analogue **esters** or their salts to cows, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) rations comprising a grain, a concentrate and a supplement containing the above **esters**/amides; and

(2) a unit dosage form comprising a 1-12C alkyl **ester** of **methionine** or its hydroxy analogue for delivering a single day's dosage of the active ingredient(s) to a cow.

MECHANISM OF ACTION - The **ester** increases/stimulates the absorption of **methionine** from the rumen preventing its premature breakdown by commensal microbes.

USE - Useful for increasing the protein, fat and volumetric content of **cow**'s milk in **dairy** and beef **cattle**. Also useful for improving rumen fermentation and the general condition of **cattle** including increasing the energy, fertility (increased fertilization rate at insemination and reduced intervals between calving) and liver function (reduction in blood ketosis and hepatic steatosis, and an improvement in very low density lipoproteins).

ADVANTAGE - The **ester**/amide allows **methionine** to pass directly from the rumen to the bloodstream improving the bioavailability of **methionine** more so than the use of hydroxy analogues of **methionine**.

Dwg.0/0

L9 ANSWER 9 OF 15 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

ACCESSION NUMBER: 2000:393434 BIOSIS

DOCUMENT NUMBER: PREV200000393434

TITLE: Effect of enzymatic modification on the biological activity and nutritive value of cow and buffalo casein.

AUTHOR(S): Hussein, S. [Reprint author]; Gelencser, E. [Reprint

author]; Polgar, M.; Hajos, Gy. [Reprint author]
CORPORATE SOURCE: Central Food Research Institute, Herman O. ut 15, H-1022, Budapest, Hungary
SOURCE: Acta Alimentaria, (September, 2000) Vol. 29, No. 3, pp. 273-287. print.
CODEN: ACALDI. ISSN: 0139-3006.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 13 Sep 2000
Last Updated on STN: 8 Jan 2002

AB Buffalo and cow milk caseins were submitted to hydrolysis either with alpha-chymotrypsin or with pepsin. Enzymatic peptide modification (EPM) was carried out by using L-**methionine** ethyl **ester** in the reaction mixture. As catalyst, alpha-chymotrypsin or pepsin was used. The incorporation of **methionine** in to the peptide chains in the presence of alpha-chymotrypsin showed an optimum value at 0.14 g **Met** added to the reaction mixture/1 g hydrolysate in both cases. In the case of pepsin used as catalyst, the optimal **Met** -enrichment was at 0.14 g **Met** added to the reaction mixture/1 g buffalo casein hydrolysate and at 0.34 g **Met**/1 g cow casein hydrolysate. The covalent nature of the amino acid incorporation was confirmed by SDS - polyacryl amide gel electrophoresis in the presence of urea. Electrophoretic patterns of the products indicate that transpeptidation plays an essential role in the EPM reaction. Antigenic character of the EPM-products was investigated in vitro by competitive indirect ELISA. Enzymatic peptide modification with **methionine** enrichment seems to be an efficient method for the reduction of the antigenic/potential allergenic character and for the improvement of the nutritive value of buffalo and cow milk caseins.

L9 ANSWER 10 OF 15 WPIDS COPYRIGHT 2004 THE THOMSON CORP on STN
ACCESSION NUMBER: 1999-142479 [12] WPIDS
DOC. NO. CPI: C1999-041551
TITLE: Ruminant food ration formulation - to provide for the **methionine** needs, particularly, of lactating **dairy cows.**
DERWENT CLASS: D13 E16 E17
INVENTOR(S): KNIGHT, C D; KOENIG, K M; RODE, L M; VANDENBERG, M J; VAZQUEZ-ANON, M
PATENT ASSIGNEE(S): (NOVU-N) NOVUS INT INC; (KNIG-I) KNIGHT C D; (KOEN-I) KOENIG K M; (RODE-I) RODE L M; (VAND-I) VANDENBERG M J; (VAZQ-I) VAZQUEZ-ANON M; (AGRI-N) AGRIFOOD CANADA
COUNTRY COUNT: 83
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9904647	A1	19990204	(199912)*	EN	43
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW					
AU 9885926	A	19990216	(199926)		
ZA 9806644	A	19990728	(199935)		41

US 6017563	A	20000125 (200012)	
EP 998203	A1	20000510 (200027)	EN
R: BE DE DK ES FR GB IE IT LU MC NL PT			
US 6183786	B1	20010206 (200109)	
MX 2000000810	A1	20001001 (200158)	
JP 2001514841	W	20010918 (200169)	37
US 6319525	B1	20011120 (200174)	
US 2002058085	A1	20020516 (200237)	
EP 1354521	A1	20031022 (200370)	EN
R: BE DE DK ES FR GB IE IT LU MC NL PT			

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9904647	A1	WO 1998-US15488	19980724
AU 9885926	A	AU 1998-85926	19980724
ZA 9806644	A	ZA 1998-6644	19980724
US 6017563	A	US 1997-900414	19970725
EP 998203	A1	EP 1998-937145	19980724
		WO 1998-US15488	19980724
US 6183786	B1 Cont of	US 1997-900414	19970725
		US 1999-333095	19990615
MX 2000000810	A1	MX 2000-810	20000124
JP 2001514841	W	WO 1998-US15488	19980724
		JP 2000-503726	19980724
US 6319525	B1 Cont of	US 1997-900414	19970725
	Cont of	US 1999-333095	19990615
		US 2000-697235	20001026
US 2002058085	A1 Cont of	US 1997-900414	19970725
	Cont of	US 1999-333095	19990615
	Cont of	US 2000-697235	20001026
		US 2001-990677	20011116
EP 1354521	A1 Div ex	EP 1998-937145	19980724
		EP 2003-14691	19980724

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 9885926	A Based on	WO 9904647
EP 998203	A1 Based on	WO 9904647
US 6183786	B1 Cont of	US 6017563
JP 2001514841	W Based on	WO 9904647
US 6319525	B1 Cont of	US 6017563
	Cont of	US 6183786
US 2002058085	A1 Cont of	US 6017563
	Cont of	US 6183786
	Cont of	US 6319525
EP 1354521	A1 Div ex	EP 998203

PRIORITY APPLN. INFO: US 1997-900414 19970725; US 1999-333095 19990615; US 2000-697235 20001026; US 2001-990677 20011116

AN 1999-142479 [12] WPIDS

AB WO 9904647 A UPAB: 19990324
Formulation of a ruminant food ration is effected by (a) determining the **methionine** needs of the ruminant; (b) identifying a plurality of natural or synthetic feed ingredients and the nutrient composition of each, including 2-hydroxy-4-(methylthio)butanoic acid or a salt, amide or **ester** of this; and (c) formulating a ration from the identified feed ingredients to meet the determined **methionine** need, comprising (i) one or more grains; (ii) a hydroxy analog of **methionine**; and (ii) optionally a bypass fat. The hydroxy analog of **methionine** is selected from 2-hydroxy-4-(methylthio)butanoic acid and its salts, amide or **ester**. It is added separately from any bypass fat added. The ration is formulated on the basis that at least 20% of the hydroxy analog of **methionine** is assumed to be available for absorption by the ruminant.

USE - The preferred formulation is particularly useful for lactating cows (claimed).

ADVANTAGE - In this process it is unnecessary to coat **methionine** or otherwise protect it from rumen microflora. Thus there is no loss of activity on mastication or cud chewing. A predictable milk response is obtained in this process. Use of the ration avoids providing excess levels of fats or other non-essential amino acids in order to satisfy the **methionine** requirement. The food ration yields a cost improvement over previous formulations, as the hydroxy analog of **methionine** is the most economical means to provide needed **methionine** to the ruminant. Use of this formulation is also advantageous to herd health and production in the dairy farm industry.

Dwg.0/12

L9 ANSWER 11 OF 15 JICST-EPlus COPYRIGHT 2004 JST on STN

ACCESSION NUMBER:	950520874 JICST-EPlus
TITLE:	Effects of Yeast Culture Supplement on Milk Protein Yield, Ruminal Fermentation, and Blood Components in Early- to Mid-lactation **Dairy Cows**.
AUTHOR:	KOBAYASHI TAKERU; ODA SHUJI; TAKENATA AKIO; ITABASHI HISAO
CORPORATE SOURCE:	Minist. of Agric., For. and Fish., Natl. Inst. of Anim. Ind.
SOURCE:	Chikusan Shikenjo Kenkyu Hokoku (Bulletin of National Institute of Animal Industry), (1995) no. 55, pp. 13-20. Journal Code: G0830A (Fig. 1, Tbl. 5, Ref. 12) CODEN: CSKKAQ; ISSN: 0077-488X
PUB. COUNTRY:	Japan
DOCUMENT TYPE:	Journal; Article
LANGUAGE:	Japanese
STATUS:	New

AB Eight Holstein cows were used in a 30 weeks lactation trial to study the effects of dietary yeast culture on milk production and composition, ruminal fermentation and blood parameters. The control diet consisted of 50% corn silage(early lactation, 3-15 weeks post parturition) or Italian ryegrass silage(mid lactation, 16-30 week post parturition) and 50% concentrate(DM basis). At 3-wk post parturition, cows were assigned in equal numbers to either 0 or 10g/d of yeast culture, Saccharomyces cerevisiae plus growth medium. Milk production in early lactation(25.4 vs. 27.7kg/d) and in mid lactation(19.3 vs. 21.4kg/d) tended to increase following the supplementation of the dietary yeast culture. Milk fat production tended to decrease with the yeast culture supplement in both

lactation periods, whereas milk protein production increased above the control by a mean of 5% in early lactation and a mean of 8% in mid lactation. The concentration and molar proportion of volatile fatty acids and the concentrations of ammonia-N in ruminal fluid were not different between treatments in each of the experimental periods. The concentrations of glucose, urea-N and non-esterified fatty acid in blood plasma were unchanged, but the concentrations of free **methionine**, arginine, lysine and isoleucine in blood plasma were significantly higher in early lactation cows fed the yeast culture, suggesting a greater rate of essential amino acids absorption in these cows. (author abst.)

L9 ANSWER 12 OF 15 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 92:647863 SCISEARCH
THE GENUINE ARTICLE: JV824
TITLE: INDUCTION OF FATTY LIVER IN COWS BY ETHIONINE ADMINISTRATION AND CONCOMITANT DECREASES OF SERUM APOLIPOPROTEINS B-100 AND A-I CONCENTRATIONS
AUTHOR: UCHIDA E; KATOH N (Reprint); TAKAHASHI K
CORPORATE SOURCE: NATL INST ANIM HLTH, HOKKAIDO BRANCH LAB, HITSUJIGAOKA 4, SAPPORO 062, JAPAN; RAKUNO GAKUEN UNIV, DEPT VET INTERNAL MED, EBETSU 069, JAPAN
COUNTRY OF AUTHOR: JAPAN
SOURCE: AMERICAN JOURNAL OF VETERINARY RESEARCH, (NOV 1992) Vol. 53, No. 11, pp. 2035-2042.
ISSN: 0002-9645.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: AGRI
LANGUAGE: ENGLISH
REFERENCE COUNT: 26
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Ethionine, an analogue of **methionine**, induces fatty liver in rats by inhibiting protein synthesis, including that of apolipoproteins in liver. Ethionine was administered to cows to elucidate the participation in fatty liver development of impaired triglyceride secretion from liver attributable to decreased apolipoprotein synthesis. The administration resulted in a significant increase of liver triglyceride contents. Several apolipoproteins were found to have decreased concentrations. In particular, apolipoprotein B-100 in very low-density (0.95 to 1.006 g/ml) lipoprotein and in low-density (1.006 to 1.063 g/ml) lipoprotein fractions was greatly reduced. The decreases of apolipoprotein B-100 concentrations in the 2 lipoprotein fractions were at least partly correlated to the decreased triglyceride concentrations in the respective fractions. Decreased concentrations of apolipoprotein A-I in high-density (1.063 to 1,210 g/ml) lipoprotein were also observed, although not as distinctly as with apolipoprotein B-100. Total cholesterol and phospholipid concentrations in low- and high-density lipoprotein fractions were decreased. The decrease in cholesterol was attributed to reduced concentrations of cholesteryl **esters**. It was suggested that the impaired lipid secretion from liver attributable to the decreased apolipoprotein concentrations has a role in ethionine-induced fatty liver of cows.

L9 ANSWER 13 OF 15 JICST-EPlus COPYRIGHT 2004 JST on STN
ACCESSION NUMBER: 890363155 JICST-EPlus
TITLE: Influence of DL-**methionine** on milk yield, milk

components, reproductivity, blood properties, etc.
AUTHOR: ISHIHARA TAKESHI; TSUNODA TAKAO; TAKEUCHI KENJI; SHIMIZU HIROMICHI; OTA KIYOSUKE; FURUNO NAOSHI; HORIGUCHI TAKAO
CORPORATE SOURCE: Hokkaidokushirochikunogyokyosaikumiai Hamanakashisho
SOURCE: Kachiku Shinryo (Journal of Veterinary Clinic), (1989) no. 312, pp. 17-22. Journal Code: X0028A (Fig. 8, Tbl. 4, Ref. 13)
ISSN: 0287-0754
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
LANGUAGE: Japanese
STATUS: New

L9 ANSWER 14 OF 15 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 83216287 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6854731
TITLE: Concentrations of methicillin in blood, normal milk and mastitic milk of cows after intramuscular injection of methicillin and tamethicillin.
AUTHOR: Ziv G; Soback S; Bor A
SOURCE: Journal of veterinary pharmacology and therapeutics, (1983 Mar) 6 (1) 41-7.
Journal code: 7910920. ISSN: 0140-7783.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198307
ENTRY DATE: Entered STN: 19900319
Last Updated on STN: 19900319
Entered Medline: 19830708

AB Tamethicillin (TAM) is a basic **ester** pro-drug of methicillin (**MET**) which is converted in the body by non-specific esterases to **MET**. Equal doses of **MET** and TAM were administered intramuscularly in a crossover trial involving four **dairy cows**. Acute mastitis was induced in each cow by infusing two quarters of the udder with Escherichia coli endotoxin 3 h before antibiotic administration. Peak serum **MET** concentrations after **MET** injection were significantly (P less than 0.001) higher than peak serum drug concentrations after TAM injection. The t1/2 of **MET** in serum after **MET** and TAM treatments were 18 min and 2 h, respectively. Normal milk **MET** concentrations during the first 8 h after TAM administration were significantly (P less than 0.05) higher than after **MET** treatment. Mastitic milk **MET** concentrations during the period 2-6 after **MET** injection were significantly (P less than 0.01) higher than after TAM administration. However, **MET** concentrations which were equal to or higher than the minimal inhibitory concentrations for penicillin G-resistant staphylococci were maintained in the mastitic milk for 8 h after treatment with **MET** and TAM.

L9 ANSWER 15 OF 15 CABA COPYRIGHT 2004 CABI on STN
ACCESSION NUMBER: 74:63632 CABA
DOCUMENT NUMBER: 19741418250
TITLE: The metabolism of glucose, acetate, lipids and amino acids in lactating **dairy cows**

AUTHOR: Bickerstaffe, R.; Annison, E. F.; Linzell, J. L.
CORPORATE SOURCE: Unilever Research Lab., Colworth House, Sharnbrook, Bedford, UK.
SOURCE: Journal of Agricultural Science, UK, (1974) Vol. 82, pp. 71-85.
DOCUMENT TYPE: Journal
LANGUAGE: English
ENTRY DATE: Entered STN: 19941101
Last Updated on STN: 19941101

AB Specialized techniques, previously used in surgically prepared goats, which simultaneously measure udder metabolism (arteriovenous difference of milk precursors X udder blood flow) and the whole body turnover of the milk precursors, have been successfully transferred to **dairy cows**. Methods of obtaining representative samples of arterial and mammary venous blood and of measuring udder blood flow are described. The rates of entry into the circulation, as indicated by isotope dilution, of glucose, acetate and plasma free fatty acids were 3.3 to 4.0, 1.7 to 2.1 and 0.5 kg/day. Acetate and glucose contributed 32 to 50 and 4 to 11%, respectively, of the total CO2 output by the animal. Measurement of the uptake of precursors of milk constituents and their transfer into milk showed that there were substantial arteriovenous differences of glucose, acetate, triglyceride and beta -hydroxybutyrate which were not significantly different between breeds or related to milk yield. Isotopic and balance data confirm that glucose is the main precursor of lactose and that the oxidation and transfer of glucose into lactose accounted for 69 to 98% of the glucose entry rate. As in the goat, plasma triglycerides and blood acetate accounted for 35 to 80% and 25 to 50% of the milk triglycerides, respectively. Propionate was extracted from plasma but the uptake was only about 8% of the value for acetate. There was no net arteriovenous difference of phospholipids, cholesterol **esters** or free fatty acids, but the fall in specific radioactivity of free fatty acids across the mammary gland indicated there was an exchange of free fatty acids between plasma and mammary tissue. In agreement with previous findings, acetate contributed to all the milk fatty acids up to a chain length of C14 and part of the C16 fatty acid. Plasma triglycerides contributed to the remainder of the C16 fatty acid and all the milk fatty acids with a chain length of C18 or higher. In contrast to the lactating goat, **cow** plasma contained very few chylomicrons. Most of the triglycerides taken up by the udder were derived from the low-density lipoprotein fraction. The essential amino acids were extracted from blood in amounts sufficient to account for the essential amino acids secreted into milk protein. Although the plasma content of **methionine** was low, 52 to 72% of the material reaching the mammary gland was taken up. The uptake of arginine was far in excess of the requirement for milk protein synthesis.

(FILE 'MEDLINE' ENTERED AT 15:39:00 ON 14 OCT 2004)

L10	219467	SEA	FILE=MEDLINE ABB=ON	PLU=ON	CATTLE/CT
L11	17169	SEA	FILE=MEDLINE ABB=ON	PLU=ON	METHIONINE/CT
L12	654	SEA	FILE=MEDLINE ABB=ON	PLU=ON	L10 AND L11
L13	9304	SEA	FILE=MEDLINE ABB=ON	PLU=ON	ESTERS/CT
L14	3	SEA	FILE=MEDLINE ABB=ON	PLU=ON	L12 AND L13

L14 ANSWER 1 OF 3 MEDLINE on STN
ACCESSION NUMBER: 87165668 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3558270

TITLE: Analysis of amino acids by gas chromatography as the N-trifluoroacetyl n-butyl esters.
AUTHOR: Gehrke C W; Kuo K C; Kaiser F E; Zumwalt R W
SOURCE: Journal - Association of Official Analytical Chemists, (1987 Jan-Feb) 70 (1) 160-70.
Journal code: 7505559. ISSN: 0004-5756.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198705
ENTRY DATE: Entered STN: 19900303
Last Updated on STN: 20000303
Entered Medline: 19870518
ED Entered STN: 19900303
Last Updated on STN: 20000303
Entered Medline: 19870518
AB This presentation describes amino acid analysis with the gas chromatographic method and experimental conditions using the N-trifluoroacetyl n-butyl ester derivatives; the study we describe here was undertaken to compare gas chromatographic (GC) and ion-exchange chromatographic (IEC) analyses of amino acids in hydrolysates of 9 diverse sample types to gain insight into effects of these 2 chromatographic methods of analysis on variation in amino acid results. Our study showed that values for samples prepared by 2 separate laboratories using the same procedure were generally in good agreement when all of the hydrolysates were analyzed by a single laboratory using a single method of analysis. To compare results from gas chromatography with those from ion-exchange chromatography analyses were performed by 2 different laboratories on the same hydrolysates and on different hydrolysates prepared by the same method by both laboratories. The data demonstrate that GC and IEC can be expected to yield essentially identical results when applied to the same hydrolysate. Agreement is so close that interlaboratory differences in hydrolysate preparation of the same sample contribute as much to variation in amino acid results as does the method of analysis, a fact which should be noted in planning collaborative studies.

L14 ANSWER 2 OF 3 MEDLINE on STN
ACCESSION NUMBER: 72104594 MEDLINE
DOCUMENT NUMBER: PubMed ID: 5168210
TITLE: Iodine, hemin and heminester as oxidants in a synthesis of ATP from ADP and P i mediated by thiols and disulfides.
AUTHOR: Bauerlein E; Klingenfuss M; Wieland T
SOURCE: European journal of biochemistry / FEBS, (1971 Dec) 24 (2) 308-12.
Journal code: 0107600. ISSN: 0014-2956.
PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197204
ENTRY DATE: Entered STN: 19900310
Last Updated on STN: 19970203
Entered Medline: 19720418
ED Entered STN: 19900310
Last Updated on STN: 19970203

Entered Medline: 19720418

L14 ANSWER 3 OF 3 MEDLINE on STN
ACCESSION NUMBER: 71036884 MEDLINE
DOCUMENT NUMBER: PubMed ID: 5529715
TITLE: The susceptibility of N-acetyl-S-alkyl- and N-acetyl-S-aryl-cysteine ethyl esters to chymotryptic hydrolysis.
AUTHOR: Damoglou A P; Lindley H; Stapleton I W
SOURCE: Biochemical journal, (1970 Jul) 118 (4) 553-6. Journal code: 2984726R. ISSN: 0264-6021.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197101
ENTRY DATE: Entered STN: 19900101
Last Updated on STN: 19970203
Entered Medline: 19710113
ED Entered STN: 19900101
Last Updated on STN: 19970203
Entered Medline: 19710113

(FILE 'CAPLUS' ENTERED AT 15:42:44 ON 14 OCT 2004)
L1 1 SEA FILE=REGISTRY ABB=ON PLU=ON "METHIONINE, METHYL ESTER"/CN

L2 2 SEA FILE=REGISTRY ABB=ON PLU=ON METHIONINE/CN
L3 1 SEA FILE=REGISTRY ABB=ON PLU=ON 4510-08-1/RN
L4 660 SEA FILE=CAPLUS ABB=ON PLU=ON L1 OR (METHIONINE OR MET)(3A)((ME OR METHYL)(W)ESTER)
L5 242 SEA FILE=CAPLUS ABB=ON PLU=ON L3 OR (METHIONINE OR MET)(W)AMIDE OR METHIONAMIDE
L15 3448 SEA FILE=CAPLUS ABB=ON PLU=ON (L2 OR MET OR METHIONINE)(L)ESTER
L16 81 SEA FILE=CAPLUS ABB=ON PLU=ON (L4 OR L5 OR L15)(L)(COW OR CATTLE OR BOVINE OR (BOS OR B)(W)TAURUS)
L17 15 SEA FILE=CAPLUS ABB=ON PLU=ON L16(L)(METHOD OR TECHNIQUE)

L18 15 L17 NOT L7

L18 ANSWER 1 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 23 May 2002
ACCESSION NUMBER: 2002:382111 CAPLUS
DOCUMENT NUMBER: 137:121155
TITLE: Dynamic docking and electron transfer between Zn-myoglobin and cytochrome b5
AUTHOR(S): Liang, Zhao-Xun; Nocek, Judith M.; Huang, Kai; Hayes, Ryan T.; Kurnikov, Igor V.; Beratan, David N.; Hoffman, Brian M.
CORPORATE SOURCE: Department of Chemistry, Northwestern University, Evanston, IL, 60208, USA
SOURCE: Journal of the American Chemical Society (2002), 124(24), 6849-6859
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal

LANGUAGE: English
OTHER SOURCE(S): CASREACT 137:121155
AB The authors present a broad study of the effect of neutralizing the two neg. charges of the Mb propionates on the interaction and electron transfer (ET) between horse Mb and **bovine** cyt b5, through use of Zn-substituted Mb (ZnMb, (1)) to study the photoinitiated reaction, (3ZnP)Mb + Fe3+cyt b5 → (ZnP)+Mb + Fe2+cyt b5. The charge neutralization has been carried out both by replacing the Mb heme with zinc-deuteroporphyrin di-Me **ester** (ZnMb(dme), (2)), which replaces the charges by small neutral hydrophobic patches, and also by replacement with the newly prepared zinc-deuteroporphyrin diamide (ZnMb(diamide), (3)), which converts the charged groups to neutral, hydrophilic ones. The effect of propionate neutralization on the conformation of the zinc-porphyrin in the Mb heme pocket has been studied by multinuclear NMR with an 15N labeled zinc porphyrin derivative (ZnMb(15N-diamide), (4)). The rates of photoinitiated ET between the Mb's (1-3) and cyt b5 have been measured over a range of pH values and ionic strengths. Isothermal titration calorimetry (ITC) and NMR **methods** have been used to independently investigate the effect of charge neutralization on Mb/b5 binding. The neutralization of the two heme propionates of ZnMb by formation of the heme diester or, for the first time, the diamide increases the second-order rate constant of the ET reaction between ZnMb and cyt b5 by as much as several 100-fold, depending on pH and ionic strength, while causing negligible changes in binding affinity. Brownian dynamic (BD) simulations and ET pathway calcns. provide insight into the protein docking and ET process. The results support a new "dynamic docking" paradigm for protein-protein reactions in which numerous weakly bound conformations of the docked complex contribute to the binding of cyt b5 to Mb and Hb, but only a very small subset of these are ET active, and this subset does not include the conformations most favorable for binding; the Mb surface is a large "target" with a small "bullseye" for the cyt b5 "arrow". This paradigm differs sharply from the more familiar, "simple" docking within a single, or narrow range of conformations, where binding strength and ET reactivity increase in parallel. Likewise, it is distinct from, although complementary to, the well-known picture of conformational control of ET through "gating", or a related picture of "conformational coupling". The new model describes situations in which tight binding does not correlate with efficient ET reactivity, and explains how it is possible to modulate reactivity without changing affinity. Such "decoupling" of reactivity from binding clearly is of physiol. relevance for the reduction of **met**-Mb in muscle and of **met**-Hb in a red cell, where tight binding of cyt b5 to the high concentration of ferrous-Mb/Hb would prevent the cytochrome from finding and reducing the oxidized proteins; it likely is of physiol. relevance in other situations, as well.
REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 2 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 08 Oct 2000
ACCESSION NUMBER: 2000:708967 CAPLUS
DOCUMENT NUMBER: 134:130567
TITLE: Effect of enzymatic modification on the biological activity and nutritive value of cow and buffalo casein
AUTHOR(S): Hussein, S.; Gelencser, E.; Polgar, M.; Hajos, G. Y.

CORPORATE SOURCE: Central Food Research Institute, Budapest, H-1022, Hung.
SOURCE: Acta Alimentaria (2000), 29(3), 273-287
CODEN: ACALDI; ISSN: 0139-3006
PUBLISHER: Akademiai Kiado
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Buffalo and **cow** milk caseins were submitted to hydrolysis either with α-chymotrypsin or with pepsin as catalyst. Enzymic peptide modification (EPM) was carried out by using L-**methionine** Et **ester** in the reaction mixture The incorporation of **methionine** into the peptide chains in the presence of α-chymotrypsin showed an optimum value at 0.14 g **Met** added to the reaction mixture/L g hydrolyzate in both cases. In the case of pepsin used as catalyst, the optimal **Met**-enrichment was at 0.14 g **Met** added to the reaction mixture/L g buffalo casein hydrolyzate and at 0.34 g **Met**/L g **cow** casein hydrolyzate. The covalent nature of the amino acid incorporation was confirmed by SDS-PAGE in the presence of urea. Electrophoretic patterns of the products indicate that transpeptidation plays an essential role in the EPM reaction. Antigenic character of the EPM-products was investigated in vitro by competitive indirect ELISA. Enzymic peptide modification with **methionine** enrichment seems to be an efficient **method** for the reduction of the antigenic/potential allergenic character and for the improvement of the nutritive value of buffalo and **cow** milk caseins.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 3 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 26 May 2000
ACCESSION NUMBER: 2000:351318 CAPLUS
DOCUMENT NUMBER: 132:333748
TITLE: A method for supplying bio-available methionine to a cow
INVENTOR(S): Robert, Jean-Claude; Bennett, Robert; Gros, Georges
PATENT ASSIGNEE(S): Rhone-Poulenc Animal Nutrition S.A., Fr.
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000028835	A1	20000525	WO 1999-EP9021	19991110

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,

CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2785772	A1	20000519	FR 1998-14249	19981113
FR 2785772	B1	20001215		
FR 2785773	A1	20000519	FR 1999-10050	19990729
FR 2785773	B1	20010420		
BR 9915290	A	20010807	BR 1999-15290	19991110
TR 200101323	T2	20010821	TR 2001-200101323	19991110
EP 1128738	A1	20010905	EP 1999-972074	19991110
EP 1128738	B1	20040512		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002529108	T2	20020910	JP 2000-581896	19991110
NZ 511427	A	20030725	NZ 1999-511427	19991110
AT 266323	E	20040515	AT 1999-972074	19991110
EP 1442664	A1	20040804	EP 2004-10767	19991110
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
US 6221909	B1	20010424	US 1999-438521	19991112
US 2001008904	A1	20010719	US 2001-794347	20010228
US 6372788	B1	20020416		
ZA 2001003539	A	20020802	ZA 2001-3539	20010502
NO 2001002355	A	20010713	NO 2001-2355	20010511
US 2002103258	A1	20020801	US 2002-60327	20020201
US 6528541	B2	20030304		
US 2003143260	A1	20030731	US 2003-336912	20030106
PRIORITY APPLN. INFO.:			FR 1998-14249 A	19981113
			FR 1999-10050 A	19990729
			EP 1999-972074 A3	19991110
			WO 1999-EP9021 W	19991110
			US 1999-438521 A1	19991112
			US 2001-794347 A1	20010228
			US 2002-60327 A1	20020201

AB A **method** for supplying bio-available **methionine** to a **cow** is described which comprises supplying to the **cow** an **ester** of **methionine** or **methionine amide** and/or an **ester** of the hydroxy analog of **methionine** or a salt thereof.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 30 Sep 1996
ACCESSION NUMBER: 1996:580085 CAPLUS
DOCUMENT NUMBER: 125:222453
TITLE: Preparation of peptide derivatives as antioxidants and antibacterial and antifungal agents
INVENTOR(S): Kawashima, Takuji; Shimamura, Seiichi; Kawase, Kozo; Takase, Mitsunori; Uein, Beramii; Hashimoto, Koichi; Wakabayashi, Hiroyuki; Matsumoto, Hiroshi; Nakamura, Hirohiko
PATENT ASSIGNEE(S): Morinaga Milk Industry Co Ltd, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 10 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 08176190	A2	19960709	JP 1994-322762	19941226

PRIORITY APPLN. INFO.: JP 1994-322762 19941226
OTHER SOURCE(S): MARPAT 125:222453

AB Lactoferrin-derived peptide derivs. R1-X, X-R2, and R1-X-R2 (R1 = Ac, acyl, polyethylene glycol; X = peptide having one of peptide sequences Arg-Arg-Trp-Gln-Trp-Arg, Arg-Arg-Trp-Gln-Trp-Arg-**Met**-Lys-Lys, Lys-Lys-Trp-Gln-Trp-Lys-**Met**-Lys-Lys, and Phe-Lys-Cys-Arg-Arg-Trp-Gln-Trp-Arg-**Met**-Lys-Lys-Leu-Gly-Ala-Pro-Ser-Ile-Thr-Cys-Val-Arg-Arg-Ala-Phe each consisting of D- or L-amino acids; R2 = NH2, acyl, polyethylene glycol), which are antioxidants suppressing active oxygen, free radicals, and peroxidn. of lipids, or were prepared either by hydrolysis of **cow** lactoferrin in the presence of pig pepsin followed by HPLC purification to give a peptide disulfide H-Phe-Lys-Cys-Arg-Arg-Trp-Gln-Trp-Arg-**Met**-Lys-Lys-Leu-Gly-Ala-Pro-Ser-Ile-Thr-Cys-Val-Arg-Arg-Ala-Phe-OH (Cys3 and Cys20 are linked by a disulfide bond) (I) or by the solid phase **method** using a Pharmacia LKB Biolynx 4170-peptide synthesizer, a NovaSyn KR resin, and Fmoc-protected amino acids and their perfluorophenyl active **esters** such as Fmoc-Lys(Boc)-OPfp (Pp = perfluorophenyl), Fmoc-Trp(Boc)-OPfp, Fmoc-Gln-OPfp, and Fmoc-**Met**-OPfp. N-stearoyl-Arg-Arg-Trp-Gln-Trp-Arg-**Met**-Lys-Lys-OH (II) in vitro inhibited peroxidn. of a liposome of egg yolk phospholipid with FeNH4(SO4)2.12H2O by 16.2, 75.7, and 88.7% at 1, 10, and 100 μg/L, resp. I and II showed min. inhibitory concentration of 6 and ≤3 μg/mL against Escherichia coli IID 861, resp. The antibacterial activity of II was completely retained after treatment with protease of Trichophyton mentagrophytes TIMM-1189, whereas I completely lost its activity. A tablet containing II, a chewing gum containing Ac-Lys-Lys-Trp-Gln-Trp-Lys-**Met**-Lys-Lys-OH, and a hand lotion containing Ac-Arg-Arg-Trp-Gln-Trp-Arg-**Met**-Lys-Lys-OH **ester** with ethylene glycol were formulated.

L18 ANSWER 5 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 24 Dec 1994
ACCESSION NUMBER: 1994:701329 CAPLUS
DOCUMENT NUMBER: 121:301329
TITLE: Preparation of peptide or its derivative and conjugate with protein and production of anti-endothelin-1 antibody using them as antigens
INVENTOR(S): Higuchi, Akihiro; Hayashi, Takashi; Baba, Kenzo
PATENT ASSIGNEE(S): Hitachi Chemical Co Ltd, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 8 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 06157592	A2	19940603	JP 1992-313269	19921124

PRIORITY APPLN. INFO.: JP 1992-313269 19921124

AB Three antigenic determinant peptide fragments of endothelin-1, H-Ser-Ser-Leu-**Met**-Asp-Lys-Glu-OH (I), H-Ser-Ser-Leu-**Met**-Asp-Lys-OH (II), and H-Ser-Leu-**Met**-Asp-Lys-Glu-OH (III), which are optionally protected at the side chain OH group and the terminal or side chain NH2 or CO2H group, and conjugates of protein with I - III peptide or its derivative are prepared Anti-endothelin-1 antibody is produced by immunization of an animal with peptides I -III or derives. or protein conjugates thereof. Peptides I - III and derivs. lack the physiol. activities of endothelin-1 such hypertension and vascular smooth muscle contraction and are useful not only as antigens for production of anti-endothelin-1 antibody specifically binding to the antigenic determinant (loop between the 3rd and 11th cysteine) of endothelin-1 but also as ligands for purification and detection of anti-endothelin-1 antibody.

Screening of antigenic determinants of endothelin-1 using 10 peptide fragments of endothelin-1 showed that II and III had the highest binding affinity to anti-endothelin-1 polyclonal antibody. Thereby, Ac-Ser-Ser-Leu-**Met**-Asp-Lys-Glu-OH (IV) was prepared by the solid phase **method** using a peptide synthesizer (model 9,050; Milligen/Biosearch) and N-Fmoc-protected amino acid pentafluorophenyl or dihydroxybenzotriazine active **esters**; protein conjugates of IV with keyhole limpet hemocyanin (KLH) and **bovine** serum albumin (BSA) were prepared by condensation of IV with each protein in the presence of n-hydroxysulfosuccinimide and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide in 50 mM KH2PO4 buffer (pH 7.0). Binding affinity of these latter conjugates to anti-endothelin-1 rabbit antibody was .apprx.60% that of the conjugates of endothelin-1 with KLH and ABS, indicating that .apprx.60% of this antibody recognizes the partial sequence Ser-Ser-Leu-**Met**-Asp-Lys-Glu of endothelin-1. Surprisingly anti-endothelin-1 mouse antibody did not bind to IV conjugate with KLH, whereas it bound to the KLH-endothelin-1 conjugate.

L18 ANSWER 6 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 14 Dec 1991
ACCESSION NUMBER: 1991:651669 CAPLUS
DOCUMENT NUMBER: 115:251669
TITLE: A method for the stepwise, controlled synthesis of chemical species, particularly peptides, on protein substrates, coupled products obtained by the method, and the use of these coupled products, e.g. as vaccines
INVENTOR(S): Houen, Gunnar; Holm, Arne
PATENT ASSIGNEE(S): Den.
SOURCE: PCT Int. Appl., 106 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9108220	A1	19910613	WO 1990-DK311	19901130

W: AT, AU, BB, BG, BR, CA, CH, DE, DK, ES, FI, GB, GR, HU, JP, KP,

KR, LK, LU, MC, MG, MW, NL, NO, RO, SD, SE, SU, US
RW: AT, BE, BF, BJ, CF, CG, CH, CM, DE, DK, ES, FR, GA, GB, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG

AU 9168929	A1	19910626	AU 1991-68929	19901130
PRIORITY APPLN. INFO.:			DK 1989-6085	19891201
			WO 1990-DK311	19901130

AB Chemical species, especially peptides, are synthesized by a stepwise, controlled process using a proteinaceous substances as the synthesis substrate. The coupled products obtained by the process can be used, e.g., as vaccines, matrix materials, or carrier mols. The products, including peptides and peptide derivs., prepared by the **method** are also claimed. **Bovine** serum albumin (BSA) was placed in a silylated reaction vessel and the CO2H groups were diethylamidated before coupling glutamic acid as the Fmoc (9-fluorenylmethyloxycarbonyl) and tert-Bu protected Dhbt (3-hydroxy-3,4-dihydrobenzotriazin-4-one **ester**, blocking remaining amino groups with acetic anhydride, and sequentially coupling Fmoc- and side chain-protected Dhbt **esters** of lysine, serine, threonine, aspartic acid, **methionine**, and serine. Piperidine was used to remove the Fmoc protecting group between couplings. Side chain protection groups were removed in CH2Cl2/F3CCO2H (1:1 volume/volume) at 0°. The product had an average of 35 synthesized peptide chains per BSA mol. The coupled product was used to raise antibodies to Ser-**Met**-Asp-Thr-Ser-Lys-Glu in rabbits.

L18 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 12 May 1990

ACCESSION NUMBER:	1990:179878 CAPLUS
DOCUMENT NUMBER:	112:179878
TITLE:	Semisynthesis of Arg15, Glu15, Met15, and Nle15-aprotinin involving enzymic peptide bond resynthesis
AUTHOR(S):	Beckmann, Juergen; Mehlich, Armin; Schroeder, Werner; Wenzel, Herbert R.; Tschesche, Harald
CORPORATE SOURCE:	Fak. Chem., Univ. Bielefeld, Bielefeld, D-4800/1, Fed. Rep. Ger.
SOURCE:	Journal of Protein Chemistry (1989), 8(1), 101-13 CODEN: JPCHD2; ISSN: 0277-8033
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB The semisynthesis of homologs of aprotinin, the **bovine** pancreatic trypsin inhibitor, is described. The P1 lysine15 residue was replaced by two **method**. The first procedure, which consisted of two enzymic steps for the incorporation of other amino acids has previously been described. The second approach consisted of six steps of both enzymic and chemical nature. The modified inhibitor, in which the lysine15-alanine16 peptide bond is hydrolyzed, was used as the starting material. All carboxyl groups of the modified inhibitor were esterified with MeOH; the lysine15 Me **ester** was then selectively hydrolyzed. Afterward, lysine15 itself was split off. Arginine, glutamic acid, **methionine**, and norleucine were incorporated using water-soluble carbodiimide combined with an acylation catalyst. The Me **ester** group was used to prevent polymerization The reactive-site peptide bonds were resynthesized using either chymotrypsin or trypsin.

L18 ANSWER 8 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 14 Jun 1986
ACCESSION NUMBER: 1986:205332 CAPLUS
DOCUMENT NUMBER: 104:205332
TITLE: Chemotactic activity of collagen-like polypeptides for human peripheral blood neutrophils
AUTHOR(S): Laskin, Debra L.; Kimura, Terutoshi; Sakakibara, Shumpei; Riley, David J.; Berg, Richard A.
CORPORATE SOURCE: Dep. Pharmacol. Toxicol., Rutgers, State Univ., Piscataway, NJ, 08854, USA
SOURCE: Journal of Leukocyte Biology (1986), 39(3), 255-66
CODEN: JLBIE7; ISSN: 0741-5400
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To study the role of collagen fragments in neutrophil migration, the authors analyzed the chemotactic properties of peptide fragments of **bovine** collagen digested with bacterial collagenase or cyanogen bromide and small mol. weight synthetic polypeptides containing proline, hydroxyproline (Hyp), and glycine (Gly), the major amino acids that comprise collagen. Using the Boyden chamber and under agarose **techniques**, it was found that collagen fragments were as potent in inducing chemotaxis in neutrophils as the bacterial-derived peptide formyl-**Met**-Leu-Phe. The synthetic polytripeptides (Pro-Pro-Gly)5 and (Pro-Hyp-Gly)5 were equipotent in inducing chemotaxis, producing a maximal induction of chemotaxis at 5-10 nM. This suggests that Hyp, the unique amino acid found in collagen, is not required for chemotactic activity. Increasing the length of the synthetic tripeptide from 5 to 10 subunits decreased its chemotactic activity, while the single tripeptide subunit (Pro-Hyp-Gly)1 was the least active peptide, inducing a maximal response at 100 nM. To study the structural requirements for chemotaxis, Pro-Hyp-Gly tripeptides were synthesized with modifications at the N and C terminal ends. Addition of a Me group to the carboxyl of Gly to form an **ester** enhanced the chemotactic activity of the peptide by 50%, while substitutions on the N-terminus with an acetyl group decreased the chemotactic activity by 50%. Substitution on the N-terminus with a Boc group decreased the chemotactic activity by 100%. Thus, there are specific structural requirements for chemotaxis induced by peptides having a collagen-like sequence of amino acids.

L18 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 17 May 1986
ACCESSION NUMBER: 1986:168810 CAPLUS
DOCUMENT NUMBER: 104:168810
TITLE: Studies on peptides. CXXVIII. Application of new heterobifunctional crosslinking reagents for the preparation of neurokinin (A and B)-BSA (bovine serum albumin) conjugates
AUTHOR(S): Fujii, Nobutaka; Hayashi, Yoshio; Katakura, Shinichi; Akaji, Kenichi; Yajima, Haruaki; Inouye, Atsuko; Segawa, Tomiro
CORPORATE SOURCE: Fac. Pharm. Sci., Kyoto Univ., Kyoto, 606, Japan
SOURCE: International Journal of Peptide & Protein Research (1985), 26(2), 121-9
CODEN: IJPPC3; ISSN: 0367-8377
DOCUMENT TYPE: Journal
LANGUAGE: English

OTHER SOURCE(S): CASREACT 104:168810
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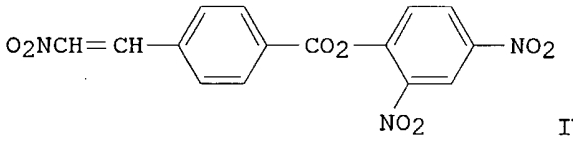

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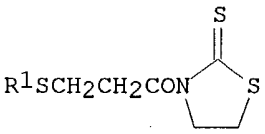
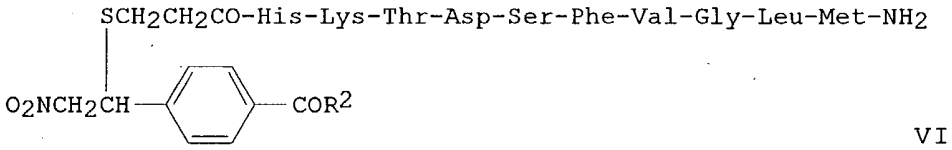


V



VI

AB Neurokinin A, R-His-Lys-Thr-Asp-Ser-Phe-Val-Gly-Leu-**Met**-NH2 (I, R = H) (II), and neurokinin B, H-Asp-**Met**-His-Asp-Phe-Phe-Val-Gly-Leu-**Met**-NH2 (III), were prepared by conventional solution **methods** and they were conjugated with **bovine** serum albumin (BSA) by heterobifunctional crosslinking reagent IV. Thus, II was treated with thiazolidine-2-thione V (R1 = Ac) to give I (R = AcSCH2CH2CO), which was deacetylated by HONH2.HCl in H2O to give I (R = HSCH2CH2CO). The addition of the latter to IV gave active **ester** VI [R2 = OC6H4(NO2)2-2,4], which was coupled with BSA to give conjugate VI (R2 = BSA). A similar conjugate of II with BSA was prepared using V (R1 = p-MeOC6H4CO) for the introduction of the SH group.

L18 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 12 May 1984
ACCESSION NUMBER: 1983:570031 CAPLUS
DOCUMENT NUMBER: 99:170031
TITLE: Intramolecular cross-linking of insulin. Preparation and properties of oxalyl- and malonyl-bis(methionyl) insulin
AUTHOR(S): Srinivasa, B. R.; Carpenter, Frederick H.
CORPORATE SOURCE: Dep. Biochem., Univ. California, Berkeley, CA, 94720, USA
SOURCE: International Journal of Peptide & Protein Research (1983), 22(2), 214-22
CODEN: IJPPC3; ISSN: 0367-8377
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The bifunctional reagents oxalylbis(**methionine**-p-nitrophenyl **ester**) [87498-79-1] and malonylbis(**methionine** -p-nitrophenyl **ester**) [87498-80-4] were prepared and investigated as reversible crosslinking reagents for insulin [9004-10-8] and model compds. The removal of the crosslinking residues was demonstrated by CNBr cleavage of oxalylbis(**Met**-Phe-OMe) [87498-81-5] and malonylbis(**Met**-Phe-OMe) [87498-82-6]. **Bovine** insulin [11070-73-8] reacted with a molar equivalent of oxalylbis(**methionine**-p-nitrophenyl **ester**) or malonylbis(

methionine-p-nitrophenyl **ester**) in the presence of excess Et3N to yield oxalyl-bis(methionyl)insulin (I) [87521-01-5] and malonyl-bis(methionyl)insulin (II) [87521-02-6], resp. In these derivs. the N-terminal phenylalanine (B1 residue) was free. Thus the crosslink was between the A1 and B29 residues in insulin. All 3 disulfide bonds of these insulin derivs. underwent reduction with Bu3P to give 6 sulfhydryls. Air oxidation of reduced I and II in 0.05M disodium phosphate, pH 9.5, yielded products which were indistinguishable from I and II, resp., as measured by physicochem. and biol. **methods**. CNBr cleavage of reduced and reoxidized II in 70% HCOOH regenerated insulin quant., but only 40% of the insulin was regenerated from similar treatment of I. The regenerated insulins exhibited the biol. activity of native insulin. The disulfide bonds formed during oxidation of reduced I and II appear to be identical to those found in insulin.

L18 ANSWER 11 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 12 May 1984
ACCESSION NUMBER: 1981:134997 CAPLUS
DOCUMENT NUMBER: 94:134997
TITLE: Semisynthesis of phospholipase A2. Preparation and properties of arginine-6 bovine pancreatic phospholipase A2
AUTHOR(S): Van Scharrenburg, Gustaaf J. M.; Puijk, Wouter C.; Egmond, Maarten R.; De Haas, Gerard H.; Slotboom, Arend J.
CORPORATE SOURCE: Lab. Biochem., State Univ. Utrecht, Utrecht, 3508 TB, Neth.
SOURCE: Biochemistry (1981), 20(6), 1584-91
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A hydrid **bovine** phospholipase A2 was prepared having arginine (Arg) at position 6. **Bovine** pancreatic prophospholipase A2 was converted into the fully ε-amidinated zymogen (AMPREC) which produced enzymically active ε-amidinated phospholipase A2 (AMPA) upon limited proteolysis. CNBr cleavage of AMPREC at the unique **methionine** (**Met**) residue at position 8 gave de-[Ala1,Met8]AMPA, a protein completely devoid of all enzymic activity. Met8 was reintroduced by coupling of the latter protein with Boc-**Met**-N-hydroxysuccinimide **ester** followed by treatment with trifluoroacetic acid yielding de-[Ala1,Gly7] AMPA. Subsequently Boc-Ala-LeuTrp(For)-Gln-Phe-Arg-Gly, synthesized by the solid-phase **technique**, was coupled, using the mixed-anhydride **method** . Removal of the protecting groups and purification gave semisynthetic [Arg6]-**bovine** AMPA in 30% yield. The feasibility of this procedure was proven unambiguously by the retroconversion of de-[Ala1,Met8]AMPA into the original **bovine** AMPA, being identical in all respects including enzymic activity with the starting AMPA. Both the affinity of [Arg6]-**bovine** AMPA for lipid-water interfaces and its ability to penetrate more densely packed monolayers of lecithin were considerably increased as compared to **bovine** AMPA. In these respects, [Arg6]-**bovine** AMPA was found to be almost identical to porcine AMPA. Moreover, [Arg6]-**bovine** AMPA possesses enhanced enzymic activity as compared to **bovine** and porcine AMPA. Thus, substitution of asparagine6 by Arg6 in **bovine** phospholipase A2

improves the binding for lipid-water interfaces. The concomitant increases in enzymic activity strongly suggests an effect of the lipid binding site on the active site.

L18 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 12 May 1984
ACCESSION NUMBER: 1979:539138 CAPLUS
DOCUMENT NUMBER: 91:139138
TITLE: Covalent attachment of amino acids to casein. 1. Chemical modification and rates of in vitro enzymic hydrolysis of derivatives
AUTHOR(S): Puigserver, Antoine J.; Sen, Lourminia C.; Gonzales-Flores, Elvira; Feeney, Robert E.; Whitaker, John R.
CORPORATE SOURCE: Dep. Food Sci. Technol., Univ. California, Davis, CA, 95616, USA
SOURCE: Journal of Agricultural and Food Chemistry (1979), 27(5), 1098-104
CODEN: JAFCAU; ISSN: 0021-8561
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Active N-hydroxysuccinimide **esters** of various tert-butyloxycarbonyl-L-amino acids were used to covalently attach amino acids to casein through isopeptide bonds. Tryptophan [73-22-3] was used to determine the best conditions for the reaction; glycine [56-40-6], alanine [56-41-7], **methionine** [**63-68-3**], N-acetylmethionine [65-82-7], aspartic acid [56-84-8], and asparagine [70-47-3] were also covalently linked to casein. In vitro rate studies performed with **bovine** α-chymotrypsin, **bovine** pancreatin, and rat bile pancreatic juice indicated that hydrolyses of the modified casein derivs. were lower than that of unmodified protein. The rates of decreased hydrolysis did not result from changes in solubility properties. but from steric hindrance as well as conformational changes of the modified protein, as shown by fluorescence and absorption spectra. The facile covalent attachment of amino acids to proteins appears to be a promising **method** for improving the biol. value of food proteins.

L18 ANSWER 13 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 12 May 1984
ACCESSION NUMBER: 1979:457544 CAPLUS
DOCUMENT NUMBER: 91:57544
TITLE: Glucagon fragment and its derivatives
INVENTOR(S): Fujino, Masahiko; Wakimasu, Mitsuhiro; Ohneda, Akira
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: Ger. Offen., 41 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2832090	A1	19790208	DE 1978-2832090	19780721

DE 2832090	C2	19890720		
JP 54024868	A2	19790224	JP 1977-88556	19770722
JP 61020560	B4	19860522		
JP 54046776	A2	19790412	JP 1977-114242	19770921
JP 61021240	B4	19860526		
US 4206199	A	19800603	US 1978-924553	19780714
FR 2398051	A1	19790216	FR 1978-21686	19780721
FR 2398051	B1	19830916		
GB 2002387	A	19790221	GB 1978-30677	19780721
GB 2002387	B2	19820210		
DE 2858718	C2	19890706	DE 1978-2858718	19780721
PRIORITY APPLN. INFO.:			JP 1977-88556	19770722
			JP 1977-114242	19770921

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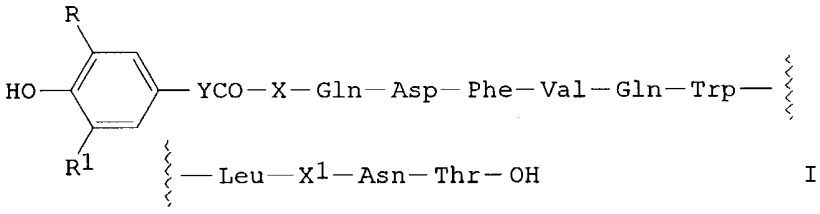

I

AB Glucagon fragments I (R, R1 = H, radioactive iodo; Y = C1-4-alkylene which can contain OH or NH2; X = peptide fragment with 1-5 amino acid residues; X1 = **Met**, Nle) were prepared as antigens for the production of antibodies specific for pancreatic glucagon. Thus, BOC-Leu-**Met**(O)-Asn-Thr-OCH2Ph (II, BOC = Me3CO2C) was BOC-deblocked and then coupled to BOC-Gln-Asp(OCH2Ph)-Phe-Val-Gln-Trp-OH (III) by dicyclohexylcarbodiimide (DCC)/N-hydroxy-5-norbornene-2,3-dicarboximide (HONB) to give the protected decapeptide, which was deblocked and then coupled to BOC-Asp(OCH2Ph)-Ser-Arg(MBS)-Arg(MBS)-Ala-OH (IV, MBS = p-MeOC6H4SO2) by DCC/HONB to give BOC-Asp(OCH2Ph)-Ser-Arg(MBS)-Arg(MBS)-Ala-Gln-Asp(OCH2Ph)-Phe-Val-Gln-Trp-Leu-**Met**(O)-Asn-Thr-OCH2Ph. The latter was deblocked with MeSO3H/anisole to give H-Asp-Ser-Arg-Arg-Ala-Gln-Asp-Phe-Val-Gln-Trp-Leu-X2-Asn-Thr-OH [V, X2 = **Met**(O)], which was reduced with thioglycolic acid to give V (X2 = **Met**) (VI). VI was coupled with the HONB **ester** of p-HOC6H4CH2CO2H to give I (R = R1 = H, Y = CH2, X = Asp-Ser-Arg-Arg-Ala, X1 = **Met**), which was treated with Na131I and chloramine T in phosphate buffer to give the corresponding iodo-131 derivative in which either one or both R1 and R2 are iodo-131. VI was also linked to **bovine** serum albumin (BSA) to give the corresponding glucagon-BSA conjugate. II, III, and IV were prepared by conventional solution **methods**.

L18 ANSWER 14 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 12 May 1984
ACCESSION NUMBER: 1979:21196 CAPLUS
DOCUMENT NUMBER: 90:21196
TITLE: A method for improving the nutritional value of food proteins: covalent attachment of amino acids
AUTHOR(S): Puigserver, Antoine J.; Sen, Lourminia C.; Clifford,

Andrew J.; Feeney, Robert E.; Whitaker, John R.
CORPORATE SOURCE: Dep. Food Sci. Technol., Univ. California, Davis, CA, USA
SOURCE: Advances in Experimental Medicine and Biology (1978), 105(Nutr. Improv. Food Feed Proteins), 587-612
CODEN: AEMBAP; ISSN: 0065-2598
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Casein was modified by use of a series of active N-hydroxysuccinimide **esters** of amino acids in order to study the effects of new covalently linked hydrophobic or hydrophilic groups on its phys. and nutritional properties. Tryptophan [73-22-3] was used to determine the best conditions for the chemical reaction and to study the stability of the newly formed amide linkage (isopeptide bond). Casein was also modified with glycine [56-40-6], alanine [56-41-7], **methionine** [**63-68-3**], N-acetylmethionine [65-82-7] and aspartic acid [56-84-8]. In vitro hydrolysis studies using **bovine** chymotrypsin, pancreatin and rat bile-pancreatic juice indicated that digestibility of the modified casein derivs. was lower than that of the untreated protein. Since solubility was not significantly changed (except for tryptophyl-casein), the decreased in vitro digestibility is probably due to other factors such as steric hindrance as well as to decrease in lysine residues available to trypsin in pancreatin and rat pancreatic juice. Plasma amino acid patterns for rats fed a 10% protein diet of highly modified glycyl-casein or methionyl-casein suggest that the ε-aminolysyl derivs. are readily hydrolyzed in vivo. This was confirmed by the growth response of rats fed the following isonitrogenous diets (protein source listed only): casein, casein + free **methionine**, methionyl-casein, casein + free N-acetylmethionine, N-acetylmethionyl-casein. Covalently attached **methionine** appeared to be as readily available as the free amino acid; bound N-acetylmethionine was also available but to a slightly lower extent. The covalent attachment of amino acids to proteins appears to be a promising **method** for improving the biol. value of food proteins.

L18 ANSWER 15 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 22 Apr 2001
ACCESSION NUMBER: 1954:80031 CAPLUS
DOCUMENT NUMBER: 48:80031
ORIGINAL REFERENCE NO.: 48:14059d-f
TITLE: Chemical studies of the proteins in activated sludge from sewage-disposal plants
AUTHOR(S): Corti, Ulrich A.
CORPORATE SOURCE: Eidg. Tech. Hochschule, Zurich, Switz.
SOURCE: Schweizerische Zeitschrift fuer Hydrologie (1953), 15, 152-7
CODEN: SZHYA6; ISSN: 0036-7842
DOCUMENT TYPE: Journal
LANGUAGE: German

AB The amino acids in the HCl hydrolyzates of fresh, centrifuged, and dried sludge were studied. The following were isolated in crystalline form by Fischer's **ester method** via the Et and iso-Pr **esters** and their purities checked by 2-dimensional paper chromatography: alanine, isoleucine, leucine, **methionine**,

phenylalanine, tyrosine, and valine. Quant. data obtained by microbiol. analysis are given for these plus arginine, glycine, histidine, lysine, serine, threonine, and cystine. Tryptophan was shown to be absent. Aspartic acid and glutamic acid were demonstrated by paper chromatography. The yield of amino acids amounted to 213.2 g. per kg. dried sludge or 30% of an ash-free basis. One lb. of activated sludge solids (from 1000 gal. sewage) has an amino-acid content qualitatively and quantitatively similar to 0.50 gal. fresh **cow** milk.

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO, CABA, AGRICOLA, VETU, VETB' ENTERED AT 15:46:18 ON 14 OCT 2004)

L19 19 S L17
L20 16 S L19 NOT L8
L21 12 DUP REM L20 (4 DUPLICATES REMOVED)

L21 ANSWER 1 OF 12 WPIDS COPYRIGHT 2004 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-191156 [18] WPIDS
DOC. NO. NON-CPI: N2004-151646
DOC. NO. CPI: C2004-075387
TITLE: Method for sterilizing a biological material e.g. tissue, blood proteins that is sensitive to radiation, involves irradiating the biological material with radiation.
DERWENT CLASS: A96 B04 C07 D22 P34
INVENTOR(S): BURGESS, W; CALVERT, G; DROHAN, W N; KENT, R S; LYNCH, T; MACPHEE, M; MANN, D; MIEKKA, S; BURGESS, W H; MACPHEE, M J; MANN, D M
PATENT ASSIGNEE(S): (BURG-I) BURGESS W; (CALV-I) CALVERT G; (DROH-I) DROHAN W N; (KENT-I) KENT R S; (LYNC-I) LYNCH T; (MACP-I) MACPHEE M; (MANN-I) MANN D; (MIEK-I) MIEKKA S; (CLEA-N) CLEARANT INC
COUNTRY COUNT: 103
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2004009137	A2	20040129	(200418)*	EN	106
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW					
US 2004033160	A1	20040219	(200418)		
AU 2003253947	A1	20040209	(200450)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004009137	A2	WO 2003-US22229	20030717
US 2004033160	A1	US 2002-197249	20020718
AU 2003253947	A1	AU 2003-253947	20030717

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003253947	A1 Based on	WO 2004009137

PRIORITY APPLN. INFO: US 2002-197249 20020718
AN 2004-191156 [18] WPIDS
AB WO2004009137 A UPAB: 20040316
NOVELTY - Sterilizing a biological material (A) that is sensitive to radiation, involves irradiating (A) with radiation under conditions such that the temperature of (A) increases during the irradiating from an initial temperature to a final temperature (Tf). The increase in the temperature of (A) is equal to the total dose of the radiation divided by the specific heat capacity of (A).

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for sterilizing (A) involving:

(a) determining the maximum acceptable temperature (Tmax) for (A) during the irradiation; and

(b) irradiating (A) with radiation such that the temperature of (A) increases during the irradiating from an initial temperature (Ti) to a final temperature to (Tf).

The Ti is not more than Tmax - T or is not more than Tmax - Tobs where T is equal to the total dose of the radiation (D) divided by the specific heat capacity (c) of the biological material and Tobs is determined by a process involving irradiating a sample of the biological material or a suitable substitute with the radiation such that (A) is to be irradiated in the step (a2) while measuring the increase in temperature of the sample.

USE - For sterilizing a biological material (e.g. dextrose, urokinase, thrombin, purified protein fraction, blood, blood cells, alpha -1 proteinase inhibitor, digestive enzymes (e.g. galactosidase or sulfatases), blood proteins (e.g. albumin, Factor VIII, Factor VII, Factor IV, fibrinogen, monoclonal immunoglobulins or polyclonal immunoglobulins) or tissue (e.g. tendons, nerves, bone, teeth, bone marrow, skin grafts, cartilage, corneas, arteries, veins, organs for transplantation, heart valves, ligaments or demineralized bone matrix), milk, or serum or plasma (e.g. fetal bovine serum or bovine serum)) that is sensitive to radiation and the sterilized biological material is useful for prophylaxis or treatment of a condition or disease in a mammal (claimed).

ADVANTAGE - The recovery of the desired activity of the biological material after sterilization by irradiation is greater than 100% of the pre-irradiation value, at least 100%, at least 90%, at least 80%, at least 70%, at least 60% or at least 50% of the pre-irradiation value. Without an adverse effect on the biological material, the method reduces the levels of at least one more active biological contaminants or pathogens contained in it e.g. viruses, bacteria (including inter- and intracellular bacteria such as mycoplasmas, urea plasmas, nanobacteria, Chlamydia, rickettsias), yeasts, molds, fungi, spores, prions or similar agents responsible alone or in combination for transmissible spongiform encephalopathies and single or multicellular parasites.

Dwg.0/3

L21 ANSWER 2 OF 12 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2003:163922 BIOSIS
DOCUMENT NUMBER: PREV200300163922
TITLE: Method for supplying bioavailable methionine to a cow.

AUTHOR(S): Robert, Jean-Claude [Inventor, Reprint Author]; Bennett, Robert [Inventor]; Gros, Georges [Inventor]
CORPORATE SOURCE: 12 rue des Mesanges, 03310 Neris les Bains, France
PATENT INFORMATION: US 6528541 March 04, 2003
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Mar 4 2003) Vol. 1268, No. 1. http://www.uspto.gov/web/menu/patdata.html. e-file. ISSN: 0098-1133 (ISSN print).
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 26 Mar 2003
Last Updated on STN: 26 Mar 2003

AB The present invention relates to a **method** for supplying bioavailable **methionine** to a **cow** which comprises supplying to the **cow** an **ester** of **methionine** or **methionine amide** and/or an **ester** of the hydroxy analogue of **methionine** or a salt thereof.

L21 ANSWER 3 OF 12 WPIDS COPYRIGHT 2004 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-708545 [67] WPIDS
CROSS REFERENCE: 2000-524535 [47]; 2001-483229 [52]; 2002-257595 [30]; 2002-351562 [38]; 2003-341083 [23]; 2003-765122 [72]; 2003-863936 [80]; 2004-041267 [04]; 2004-107099 [11]; 2004-294223 [27]
DOC. NO. NON-CPI: N2003-566188
DOC. NO. CPI: C2003-195339
TITLE: Processing of whole corn, to produce corn meal and corn oil, involves cracking, conditioning and extracting corn.
DERWENT CLASS: A97 D13 D16 D21 D23 H07 H09 X25
INVENTOR(S): AMORE, F; BEAVER, M J; FOX, E J; INGVALSON, J; JAKEL, N T; KOTOWSKI, D; PATIST, A; TUPY, M J; ULRICH, J F; ADU-PEASAH, P
PATENT ASSIGNEE(S): (RENE-N) RENESSEN LLC; (CRGI) CARGILL INC
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2003083512	A1	20030501	(200367)*		25
US 6610867	B2	20030826	(200367)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 2003083512	A1	CIP of	US 2000-637843	20000810
		CIP of	US 2001-927836	20010810
			US 2002-47725	20020115
US 6610867	B2	CIP of	US 2000-637843	20000810
		CIP of	US 2001-927836	20010810
			US 2002-47725	20020115

PRIORITY APPLN. INFO: US 2002-47725 20020115; US 2000-637843 20000810; US 2001-927836 20010810

Searcher : Shears 571-272-2528

AN 2003-708545 [67] WPIDS
CR 2000-524535 [47]; 2001-483229 [52]; 2002-257595 [30]; 2002-351562 [38]; 2003-341083 [23]; 2003-765122 [72]; 2003-863936 [80]; 2004-041267 [04]; 2004-107099 [11]; 2004-294223 [27]
AB US2003083512 A UPAB: 20040426
NOVELTY - Processing of whole corn includes cracking, conditioning, and extracting the corn to produce corn meal and corn oil. The corn is not flaked during processing.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(a) a feed ration comprising corn meal and other nutrient(s);

(b) a corn oil-containing product comprising a corn oil that contains oil extracted from germ and/or endosperm of corn, and at least one other component extracted from endosperm, tipcap, or pericarp of corn;

(c) a method of producing extracted blended meal by combining corn and other oilseed grains to form a grain mixture, cracking the mixture, conditioning the mixture, and extracting the mixture; or combining corn meal with extracted oilseed meal; and

(d) a method of producing fermentation products by combining corn meal with water and alpha -amylase enzyme, incubating the combination and adding glucoamylase or protease, and mixing the combination with microorganism capable of fermenting a carbon source to produce fermented product.

USE - For processing whole corn to produce corn meal and corn oil. The corn meal is useful as human food product, e.g. puffed snack food, cereal, chip, bread, blended food, extruded snack food, food binding agent, food supplement, nutritional food bar, multi-vitamin supplement, or porridge. The corn oil may be incorporated into an oil-containing product, e.g. food oil, cooking oil, edible oil, or blended oil or fuel; or an oil-based product, e.g. food supplement, sport drink, cereal, multi-vitamin supplement, nutritional food bar, or diet drink. (All claimed)

ADVANTAGE - The novel method reduces the number of steps in processing corn and the amount of fines produced, by eliminating the flaking step.

Dwg.0/0

L21 ANSWER 4 OF 12 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

ACCESSION NUMBER: 2002:286619 BIOSIS
DOCUMENT NUMBER: PREV200200286619
TITLE: Method for supplying bioavailable methionine to a cow.
AUTHOR(S): Robert, Jean-Claude [Inventor, Reprint author]; Bennett, Robert [Inventor]; Gros, Georges [Inventor]
CORPORATE SOURCE: Neris les Bains, France
ASSIGNEE: Rhone-Poulenc Animal Nutrition, Antony, France
PATENT INFORMATION: US 6372788 April 16, 2002
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Apr. 16, 2002) Vol. 1257, No. 3. http://www.uspto.gov/web/menu/patdata.html. e-file. CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 8 May 2002
Last Updated on STN: 8 May 2002

AB The present invention relates to a **method** for supplying bioavailable **methionine** to a **cow** which comprises

supplying to the **cow** an **ester** of **methionine** or **methionine amide** and/or an **ester** of the hydroxy analogue of **methionine** or a salt thereof.

L21 ANSWER 5 OF 12 WPIDS COPYRIGHT 2004 THE THOMSON CORP on STN
ACCESSION NUMBER: 2002-657493 [70] WPIDS
DOC. NO. NON-CPI: N2002-519835
DOC. NO. CPI: C2002-184482
TITLE: Determining the concentration of free unbound hydrophobic Coenzyme A ester useful for analyzing blood samples comprises allowing at least one species of hydrophobic Coenzyme A ester to bind to hydrophobic Coenzyme A binding construct.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): KNUDSEN, J; NEERGAARD, T B F; VILLADSEN, J; WADUM, M C T
PATENT ASSIGNEE(S): (BIOS-N) BIOSENSOR APS
COUNTRY COUNT: 95
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002061096	A1	20020808	(200270)*	EN	115
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW					
W: AE AG AL AM AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU DM DZ EC ES GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
US 2002142347	A1	20021003	(200272)		
EP 1335984	A1	20030820	(200362)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR					
AU 2002212094	A1	20020812	(200427)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002061096	A1	WO 2001-DK701	20011024
US 2002142347	A1 Provisional	US 2001-262366P	20010119
		US 2001-987108	20011113
EP 1335984	A1	EP 2001-980193	20011024
		WO 2001-DK701	20011024
AU 2002212094	A1	AU 2002-212094	20011024

FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 1335984	A1 Based on	WO 2002061096
AU 2002212094	A1 Based on	WO 2002061096

PRIORITY APPLN. INFO: US 2001-262366P 20010119; DK 2000-1683 20001110
AN 2002-657493 [70] WPIDS
AB WO 200261096 A UPAB: 20021031

NOVELTY - Determining the concentration of free unbound hydrophobic Coenzyme A ester (I) in the sample by allowing at least one species of (I) to bind to the hydrophobic Coenzyme A binding construct (II) forming a complex of (I) and (II), is new.

DETAILED DESCRIPTION - Determining the concentration of (I) comprises:

(a) providing (II) exhibiting a first signal when unbound and exhibiting a measurably different second signal when bound to (I);

(b) contacting the sample with the labeled (II);

(c) allowing at least one species of (I) to bind to (II), forming a complex of (I) and (II);

(d) detecting the signal from the complex; and

(e) correlating the signal to the concentration of at least one species of (I) in the sample.

INDEPENDENT CLAIMS are also included for the following:

(1) a construct for binding (I) comprising a heterologous peptide capable of binding at least one species of (I), and a signal moiety;

(2) a kit for detecting the concentration of (I) in the sample comprising at least a first construct according to (1), and a sample compartment for the application of the sample;

(3) a nucleotide sequence encoding the heterologous peptide according to (1);

(4) an expression vector and a cell comprising the nucleotide sequence in (3); and

(5) determining the amount of free hydrophobic carboxylic acids and/or lipid constituents in the sample, comprising:

(a) optionally fractionating the sample to obtain a substantially cell-free sample;

(b) mixing the substantially cell-free sample with an amount of water-miscible organic solvent to precipitate proteins and obtain a solution of free fatty acids; and

(c) subjecting a sample of the supernatant to a quantitative analysis determining the amount of free fatty acids in the sample.

USE - The method is useful for analyzing blood samples. The constructs are useful for measuring free acyl-CoA concentrations of physiological important, highly amphiphatic, medium and long-chain acyl-CoA esters. The kit is useful for detecting the concentration of hydrophobic Coenzyme A ester (claimed).

ADVANTAGE - The method provides an easy and convenient extraction of free hydrophobic acids and lipids with the simultaneous precipitation of proteins that may interfere with the quantitative determination. The method also provides a peptide comprised in the construct with high affinity to hydrophobic CoA esters. The KD of the construct with respect to hydrophobic CoA esters is lower in magnitude than the affinity of prior constructs used for binding of fatty acids. Due to this increased binding affinity, the interference of other potential sinks for hydrophobic CoA esters with the binding assays is markedly reduced, and a much more precise estimation of the concentration of the hydrophobic CoA esters resulted.

Dwg.0/14

L21 ANSWER 6 OF 12 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN

ACCESSION NUMBER: 2002:607877 SCISEARCH

THE GENUINE ARTICLE: 574GF

TITLE: Fluorescently labelled bovine acyl-CoA-binding protein

acting as an acyl-CoA sensor: Interaction with CoA and acyl-CoA esters and its use in measuring free acyl-CoA esters and non-esterified fatty acids

AUTHOR: Wadum M C T; Villadsen J K; Feddersen S; Moller R S; Neergaard T B F; Kragelund B B; Hojrup P; Faergeman N J; Knudsen J (Reprint)

CORPORATE SOURCE: Univ So Denmark, Dept Biochem & Mol Biol, Campusvej 55, DK-5230 Odense M, Denmark (Reprint); Univ So Denmark, Dept Biochem & Mol Biol, DK-5230 Odense M, Denmark; Univ Copenhagen, Dept Prot Chem, Inst Mol Biol, DK-1353 Copenhagen, Denmark

COUNTRY OF AUTHOR: Denmark

SOURCE: BIOCHEMICAL JOURNAL, (1 JUL 2002) Vol. 365, Part 1, pp. 165-172.
Publisher: PORTLAND PRESS, 59 PORTLAND PLACE, LONDON W1N 3AJ, ENGLAND.
ISSN: 0264-6021.

DOCUMENT TYPE: Article; Journal

LANGUAGE: English

REFERENCE COUNT: 26

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Long-chain acyl-CoA **esters** are key metabolites in lipid synthesis and beta-oxidation but, at the same time, are important regulators of intermediate metabolism, insulin secretion, vesicular trafficking and gene expression. Key tools in studying the regulatory functions of acyl-CoA **esters** are reliable **methods** for the determination of free acyl-CoA concentrations. No such **method** is presently available. In the present study. we describe the synthesis of two acyl-CoA sensors for measuring free acyl-CoA concentrations using acyl-CoA-binding protein as a scaffold. **Met**(21) and Ala(53) of **bovine** acyl-CoA-binding protein were replaced by cysteine residues, which were covalently modified with 6-bromo-acetyl-2-dimethylaminonaphthalene to make the two fluorescent acyl-CoA indicators (FACIs) FACI-24 and FACI-53. FACI-24 and FACI-53 showed fluorescence emission maximum at 510 and 525 nm respectively, in the absence of ligand (excitation 387 nm). TitRation of FACI-24 and FACI-53 with hexadecanoyl-CoA and dodecanoyl-CoA increased the fluorescence yield 5.5 and 4.7-fold at 460 and 495 nm respectively. FACI-24 exhibited a high, and similar increase in, fluorescence yield at 460 nm upon binding of C-14-C-20 saturated and unsaturated acyl-CoA **esters**. Both indicators bind long-chain (> C-14) acyl-CoA **esters** with high specificity and affinity (K-d = 0.6-1.7 nM). FACI-53 showed a high fluorescence yield for C-8-C-12, acyl chains. It is shown that FACI-24 acts as a sensitive acyl-CoA sensor for measuring the concentration of free acyl-CoA, acyl-CoA synthetase activity and the concentrations of free fatty acids after conversion of the fatty acid into their respective acyl-CoA **esters**.

L21 ANSWER 7 OF 12 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN DUPLICATE 1

ACCESSION NUMBER: 2000:636671 SCISEARCH

THE GENUINE ARTICLE: 344QB

TITLE: Effect of enzymatic modification on the biological activity and nutritive value of cow and buffalo casein

AUTHOR: Hussein S (Reprint); Gelencser E; Polgar M; Hajos G

CORPORATE SOURCE: CENT FOOD RES INST, HERMAN O UT 15, H-1022 BUDAPEST,

HUNGARY (Reprint)
COUNTRY OF AUTHOR: HUNGARY
SOURCE: ACTA ALIMENTARIA, (SEP 2000) Vol. 29, No. 3, pp. 273-287.
Publisher: AKADEMIAI KIADO, PO BOX 245, H-1519 BUDAPEST, HUNGARY.
ISSN: 0139-3006.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: AGRI
LANGUAGE: English
REFERENCE COUNT: 20

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Buffalo and **cow** milk caseins were submitted to hydrolysis either with alpha-chymotrypsin or with pepsin. Enzymatic peptide modification (EPM) was carried out by using L-**methionine** ethyl **ester** in the reaction mixture. As catalyst, alpha-chymotrypsin or pepsin was used. The incorporation of **methionine** in to the peptide chains in the presence of alpha-chymotrypsin showed an optimum value at 0.14 g **Met** added to the reaction mixture/1 g hydrolysate in both cases. In the case of pepsin used as catalyst, the optimal **Met**-enrichment was at 0.14 g **Met** added to the reaction mixture/1 g buffalo casein hydrolysate and at 0.34 g **Met** /1 g **cow** casein hydrolysate.

The covalent nature of the amino acid incorporation was confirmed by SDS - polyacryl amide gel electrophoresis in the presence of urea. Electrophoretic patterns of the products indicate that transpeptidation plays an essential role in the EPM reaction. Antigenic character of the EPM-products was investigated in vitro by competitive indirect ELISA.

Enzymatic peptide modification with **methionine** enrichment seems to be an efficient **method** for the reduction of the antigenic/potential allergenic character and for the improvement of the nutritive value of buffalo and **cow** milk caseins.

L21 ANSWER 8 OF 12 WPIDS COPYRIGHT 2004 THE THOMSON CORP on STN
ACCESSION NUMBER: 1992-056378 [52] WPIDS
DOC. NO. CPI: C1992-025443
TITLE: Treatment of inflammatory thrombotic and cholesterolaemic diseases - using methionine analogue opt. in conjunction with e.g. homocysteine, affecting vitamin, antioxidant and coagulation inhibitor.
DERWENT CLASS: B05 C03
INVENTOR(S): BAYLESS, R K; HIRSCH, G P
PATENT ASSIGNEE(S): (LITH-N) LITHOX CORP
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 5084482	A	19920128	(199252)*		

PRIORITY APPLN. INFO: US 1990-508104 19900410
AN 1992-056378 [52] WPIDS
AB US 5084482 A UPAB: 19931006
A **method** for inhibiting inflammatory, ischaemic, thrombotic, and cholesteraemic disease response in a subject in need of treatment,

comprises oral admin. or at least one methiomine (**Met**) cpd. which is a **Met** hydroxy analogue, a cpd. of formula MeS(CH2)nCH(NH2)COOH, an. N-(mono-or di-carboxylic acid) acyl-**Met** or an alkyl **ester** of a **Met** cpd. or analogue. n= 1-3.

USE/ADVANTAGE - The **Met** type cpds., in the dl-or d-form, at relatively high, well tolerated doses, are potent antioxidant and anti-inflammatory agents in man and animals. e.g. **Met** or S-methyl cysteine were 3 times more active (on an equimolar basis) than vitamin C as an antioxidant for HOCl, which can cause proteolysis and tissue damage. Vitamin C also has limited oral uptake, unlike **Met** . A pref. form, for inhibiting cholesteraemic disease, is as a foodstuff containing the **Met** cpd. Dosage is 1-10g/70kg/day until inflammation is relieved for humans. For dogs, **cows**, pigs, or cats, dosage is of an acyl-**Met**, 5-100mg/kg/day in foodstuffs, amount is 3-15g l-**methionine**/100g protein.

0/0

L21 ANSWER 9 OF 12 MEDLINE on STN DUPLICATE 2

ACCESSION NUMBER: 86113793 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3456007
TITLE: Chemotactic activity of collagen-like polypeptides for human peripheral blood neutrophils.
AUTHOR: Laskin D L; Kimura T; Sakakibara S; Riley D J; Berg R A
SOURCE: Journal of leukocyte biology, (1986 Mar) 39 (3) 255-66. Journal code: 8405628. ISSN: 0741-5400.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198603
ENTRY DATE: Entered STN: 19900321
Last Updated on STN: 19900321
Entered Medline: 19860326

AB Damage to interstitial connective tissue is associated with the rapid accumulation of monocytes and neutrophils at the site of injury. To study the role of collagen fragments in neutrophil migration, we analyzed the chemotactic properties of peptide fragments of **bovine** collagen digested with bacterial collagenase or cyanogen bromide and small molecular weight synthetic polypeptides containing proline (Pro), hydroxyproline (Hyp), and glycine (Gly), the major amino acids that comprise collagen. Using the Boyden chamber and under agarose **techniques**, we found that collagen fragments were as potent in inducing chemotaxis in neutrophils as the bacterial-derived peptide f-**met**-leu-phe. The synthetic polytripeptides (Pro-Pro-Gly)5 and (Pro-Hyp-Gly)5 were found to be equipotent in inducing chemotaxis, producing a maximal induction of chemotaxis at 5-10 nM. This suggests that Hyp, the unique imino acid found in collagen, is not required for chemotactic activity. Increasing the length of the synthetic tripeptide from 5 to 10 subunits decreased its chemotactic activity, while the single tripeptide subunit (Pro-Hyp-Gly)1 was the least active peptide, inducing a maximal response at 100 nM. To study the structural requirements for chemotaxis, Pro-Hyp-Gly tripeptides were synthesized with modifications at the N and C terminals ends. Addition of a methyl group to the carboxyl of Gly to form an **ester** enhanced the chemotactic activity of the peptide by 50%, while substitutions on the amino terminus with an acetyl group decreased the chemotactic activity by 50%. Substitution on the

amino terminus with a Boc group decreased the chemotactic activity by 100%. These results indicate that there are specific structural requirements for chemotaxis induced by peptides having a collagen-like sequence of amino acids.

L21 ANSWER 10 OF 12 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

ACCESSION NUMBER: 1981:231631 BIOSIS
DOCUMENT NUMBER: PREV198172016615; BA72:16615
TITLE: SEMI SYNTHESIS OF PHOSPHO LIPASE A-2 EC-3.1.1.4 PREPARATION AND PROPERTIES OF 6 ARGININE BOVINE PANCREATIC PHOSPHO LIPASE A-2.
AUTHOR(S): VAN SCHARRENBURG G J M [Reprint author]; PUIJK W C; EGMOND M R; DE HAAS G H; SLOTBOOM A J
CORPORATE SOURCE: LAB BIOCHEM, STATE UNIV UTR, TRANSITORIUM 3, UNIV CENT "DE UITHOF", PADUALAAN 8, 3508 TB UTRECHT, NETH
SOURCE: Biochemistry, (1981) Vol. 20, No. 6, pp. 1584-1591. CODEN: BICHAW. ISSN: 0006-2960.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB The major differences between porcine and **bovine** pancreatic phsopholipases A2 are the low affinity of the **bovine** enzyme for lipid-water interfaces and its low capacity to penetrate more densely packed monolayers of lecithins. In the proposed binding site for lipid-water interfaces the porcine enzyme has an Arg residue at position 6 which is Asn in the **bovine** enzyme. In order to study whether this difference affects the above-mentioned properties, a hybrid **bovine** phospholipase A2 that has Arg at position was prepared. **Bovine** pancreatic prophospholipase A2 was converted into the fully ε-amidinated zymogen (AMPREC) which produced enzymatically active ε-amidinated phoholipase A2 (AMPA) upon limited proteolysis. CNBr cleavage of AMPREC at the unique **Met** residue at positon 8 gave des(Ala1-Met8)AMPA, a protein completely devoid of all ezymatic activity. Met8 was reintroduced by coupling of the latter protein with Boc[tert-butyloxycarbonyl]-**Met**-N-hydroxysuccinimide **ester** followed by treatment with trifluoroacetic acid, yielding des(Ala1-Gly7)AMPA. Subsequently Boc-Ala-Leu-Trp(For)-Gln-Phe-Arg-Gly, synthesized by the solid-phase **technique**, was coupled by using the mixed-anhydride **method**. Removal of the protecting groups and purification gave semisynthetic **bovine** (Arg6)AMPA in 30% yield. The feasibility of this procedure was proven unambiguously by the retroconversion of des(Ala1-Met8)AMPA into the original **bovine** AMPA, being identical in all respects including enzymatic activity with the starting AMPA. The affinity of **bovine** [Arg6]AMPA for lipid-water interfaces and its ability to penetrate more densely packed monolayers of lecithin are considerably increased as compared to the **bovine** AMPA. In these respects **bovine** [Arg6]AMPA was found to be almost identical with the porcine AMPA. **Bovine** [Arg6]AMPA possesses enhanced enzymatic activity as compared to **bovine** and porcine AMPA. Apparently substitution of Asn6 by Arg in **bovine** phospholipase A2 improves the binding for lipid-water interfaces. The concomitant increase in enzymatic activity strongly suggests an effect of the lipid binding site on the active site.

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STN DUPLICATE 3

ACCESSION NUMBER: 1980:154659 BIOSIS
DOCUMENT NUMBER: PREV198069029655; BA69:29655
TITLE: COVALENT ATTACHMENT OF AMINO-ACIDS TO CASEIN 1. CHEMICAL MODIFICATION AND RATES OF IN-VITRO ENZYMATIC HYDROLYSIS OF DERIVATIVES.
AUTHOR(S): PUIGSERVER A J [Reprint author]; SEN L C; GONZALES-FLORES E; FEENEY R E; WHITAKER J R
CORPORATE SOURCE: DEP FOOD SCI TECHNOL, UNIV CALIF, DAVIS, CALIF 95616, USA
SOURCE: Journal of Agricultural and Food Chemistry, (1979) Vol. 27, No. 5, pp. 1098-1104.
CODEN: JAFCAU. ISSN: 0021-8561.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB Active N-hydroxysuccinimide **esters** of various tert-butyloxycarbonyl-L-amino acids were used to covalently attach amino acids to casein through isopeptide bonds. Tryptophan was used to determine the best conditions for the reaction; glycine, alanine, **methionine**, N-acetylmethionine, aspartic acid and asparagine were also covalently linked to casein. In vitro rate studies performed with **bovine** α-chymotrypsin, **bovine** pancreatin and rat bile pancreatic juice indicated that hydrolysis of the modified casein derivatives were lower than that of unmodified protein. The rates of decreased hydrolyses did not result from changes in solubility properties but was rather due to steric hindrance and conformational changes of the modified protein as shown by fluorescence and absorption spectra. The facile covalent attachment of amino acids to proteins appears to be a promising **method** for improving the biological value of food proteins.

L21 ANSWER 12 OF 12 MEDLINE on STN
ACCESSION NUMBER: 79079817 MEDLINE
DOCUMENT NUMBER: PubMed ID: 727027
TITLE: A method for improving the nutritional value of food proteins: covalent attachment of amino acids.
AUTHOR: Puigserver A J; Sen L C; Clifford A J; Feeney R E; Whitaker J R
SOURCE: Advances in experimental medicine and biology, (1978) 105 587-612.
Journal code: 0121103. ISSN: 0065-2598.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197902
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AB Casein was modified by use of a series of active N-hydroxy-succinimide **esters** of amino acids in order to study the effects of new covalently linked hydrophobic or hydrophilic groups on its physical and nutritional properties. Tryptophan was used to determine the best conditions for the chemical reaction and to study the stability of the newly formed amide linkage (isopeptide bond). Casein was also modified with glycine, alanine, **methionine**, N-acetyl-**methionine**

and aspartic acid. In vitro hydrolysis studies using **bovine** chymotrypsin, pancreatine and rat bile-pancreatic juice indicated that digestibility of the modified casein derivatives was lower than that of the untreated protein. Since solubility was not significantly changed (except for tryptophyl-casein), the decreased in vitro digestibility is probably due to other factors such as steric hindrance as well as decrease in lysine residues available to trypsin in pancreatin and rat pancreatic juice. Plasma amino acid patterns for rats fed a 10% protein diet of highly modified glycyl-casein or methionyl-casein suggest that the epsilon-aminolysyl derivatives are readily hydrolyzed in vivo. This was confirmed by the growth response of rats fed the following isonitrogenous diets (protein source listed only): casein, casein + free **methionine**, methionyl-casein, casein + free N-acetyl-**methionine**, N-acety-methionyl-casein. Covalently attached **methionine** appeared to be as readily available as the free amino acid; bound N-acetyl-**methionine** was also available but to a slightly lower extent. Although this study is preliminary, the covalent attachment of amino acids to proteins appears to be a promising **method** for improving the biological value of food proteins.

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